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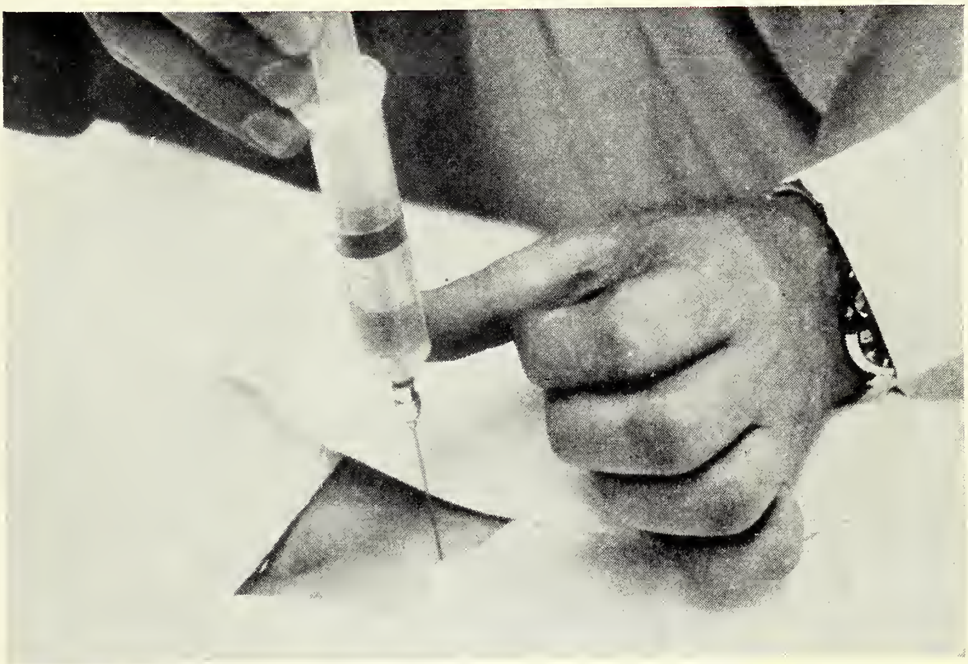

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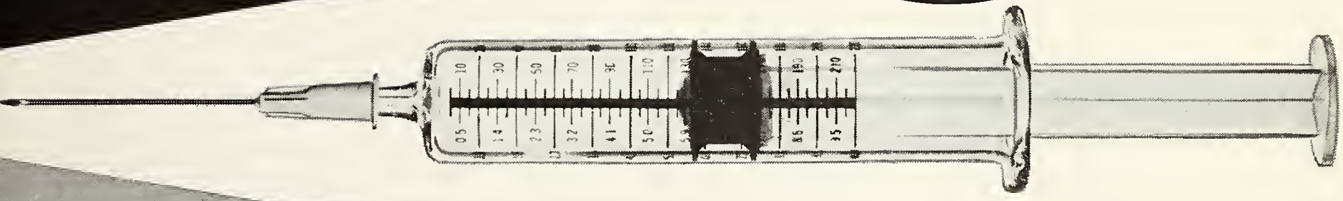

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CONTENTS

editorials

Effect Of Some Drugs On Dreaming Sleep . . . 1
Improving Cognitive Function In Senility By Hyperoxygenation 2
Genetic Factors, Serum Cholesterol And Cardiovascular Disease 6
What The Doctor Can Do In Solving The Problem Of Sudden Death . . . 8
Effect Of Alcohol On The Blood . . . 9
Horse Influenza And The Human Hong Kong Strain . . . 10
Amniocentesis In Prediction Of Chromosomal And Behavioral Abnormalities . . . 10
Education Of The Infant And Young Child . . . 12
Case Histories In Environmental Degradation . . . 14
Hazards Of Obesity . . . 16

scientific

Fetal Intrauterine Transfusion II, *Maclyn E. Wade, M.D., John A. Ogden, M.D.,* and *Clarence D. Davis, M.D.* . . . 21
Ocular (Pigmentary) Effects of Psychotropic Drugs, *William S. Appleton, M.D., Richard I. Shader, M.D.* and *Alberto DiMascio, Ph.D.* . . . 25
The Effect Of Thyroid Therapy On The Hyponatremia And Hypoosmolality Of Myxedema, *Norman J. Marieb, M.D., Edgardo P. Ragaza, M.D.,* and *Jafar Al-Sadir, M.D.* . . . 29
Methimazol Induced Aplastic Anemia, *Arthur H. Rosenberg, M.D.* . . . 32

departments

The President's Page . . . 47
From The Executive Director's Office . . . 52
Physician's Placement Service . . . 65
Woman's Auxiliary . . . 63

miscellaneous

Medical Grand Rounds—Yale-New Haven Hospital
A Case of Manic-Depressive Illness with Lithium Toxicity, *Frederick Lee Sachs, M.D.,* and *Lewis Landsberg, M.D., Editors* . . . 36
Anesthesiology Grand Rounds—Yale-New Haven Hospital
Hypothermia For Excision of Hepatic Artery Aneurysm, *Samuel M. Lerner, M.D., Allen L. Toole, M.D.,* and *Frederick W. Hehre, M.D.* . . . 40
X-Ray Of The Month, *Arnold B. Rilance, M.D.* . . . 45
Electrocardiogram Of The Month, *Hyman N. Chernoff, M.D.* . . 58
British National Health Services, *Ned Thomas* . . . 60
Around The State . . . 66
Obituary: Morris Tuch, M.D. . . . 69
In Memoriam . . . 69
Meetings . . . 70
Science News . . . 71

Connecticut Medicine

editorials

Effect of Some Drugs on Dreaming Sleep

A slow human brain change in addicts after taking amphetamine was recognized by Oswald[1] while studying their reactions to the dreaming phase of sleep (rapid eye movement phase REM). When amphetamine is first administered it suppresses this kind of sleep. However, repeated consumption leads to tolerance including a return of REM sleep to normal (20-25 percent of the total sleep). When the drug is withdrawn a "rebound" increase to more than normal REM sleep occurs especially causing REM sleep to start early in the sleep period. Data from six addicts suggested a return to normal in about three weeks, but a more careful look suggested that a full recovery was actually taking a couple of months. These observations led Oswald to postulate that a neuronal injury results from amphetamine and that recovery from this injury takes time. If this is true there should be a time scale of recovery from other drugs which affect sleep.

Barbiturates also suppress REM sleep duration and at the same time reduce the perfusion of actual eye movements. If the drugs are administered for 1-3 weeks, the effects lessen and after they are stopped a rebound of REM sleep above normal occurs, which once more lasts more than a month. The rebound in this case is coupled with spontaneous complaints of vivid and unpleasant dreams and also with more than the normal amount of eye movement during REM sleep. Here again REM sleep "rebound" has both a duration and intensity factor.

More recently Oswald and Lewis looked at REM sleep in patients who had taken overdoses of tricyclic antidepressants of the imipramine type. These drugs powerfully suppress REM sleep and after an overdose, a rebound with intense dreams again appears and recovery to normal takes a month. After heroin the REM sleep rebound persists for more than 2 months. Not all drugs that act on the central nervous system have the property of suppressing REM sleep. Some like fenfluramine have no immediate effect on REM sleep. Others like 1-tryptophan or reserpine increase REM sleep.

After electroconvulsive therapy (ECT) it takes 5-7 weeks for the EEG to return to normal. After injury to animal brains there is also a long time course for recovery. The nerve gas "Sarin" an organophosphate compound rapidly renders inactive or destroys the enzyme cholinesterase and with it the machinery for producing brain cholinesterase. The recovery process begins promptly but requires many weeks and is believed to be dependent on synthesis within the brain cells of new machinery for the production of the enzymes. Recovery from another form of insult to cerebral neurones was described by Watson[2] who injured nerve axons outside the skull. He measured the nucleic acid content of the nucleoli of the neurones concerned, for it is here that m-RNA concentrate and this is a measure of the ribosome synthesizing system of the neuron. Again recovery is on a time scale of 2 months or more while the repair synthesis is in progress.

Protein synthesis thus seems to be the basic measure by which neurones recover from drug injury. Reserpine in one large dose depletes the rabbit brain of monoamines including catecholamines which are stored in certain neurones. The reserpine disappears from the brain in a few hours. The recovery curve, however, has the familiar appearance of other forms of injury and is on a time scale of weeks.[3] It is as if the storage facilities have to be synthesized afresh.

The REM sleep "rebound" after antidepressants and heroin begin within 24 hours for it takes about a day for such substances to be eliminated from the body. However, the peak of recovery is delayed for about 10 days. The rate of increase of REM sleep seems to relate to the rate of disappearance of the particular drug from the brain and the peak of rebound seems to follow closely on the final disappearance of the drug. The increase in REM sleep after reserpine may be the result of the exceptional rapidity with which it disappears from the brain and releases the reparative processes.

The processes of repair set in motion after nerve gas, nerve injury, drugs that suppress REM sleep and reserpine which increases it, each imply protein synthesis within brain cells, a kind of process of reformation of neuronal sleep-controlling machinery through protein synthesis. Obviously the time scale of synthesis must vary with the individual protein, oxygen supply and nutrilite availability. Studies with labelled amino acids indicate a half-life for brain proteins of 3-27 days under optional conditions. In an average of 15 days we should expect a 50 percent recovery in 2 weeks and about 94 percent recovery in 2 months which is very close to what is actually seen. On the basis of such reasoning Oswald proposes that all kinds of active repair in mammalian brain cells are accompanied by an increase in REM sleep.

From observations on drug effects on neuronal activity, it is clear that sleep research offers an important tool in studying the delayed processes involved in neuronal repair machinery. Certain monoamine oxidase inhibitors (MOAI) such as phenelzine lead to total inhibition of REM sleep which can last for many weeks and is accompanied by improvement in mood rather than psychic deterioration as happens in dream deprivation from other sources. However, the eventual withdrawal of MAOI does cause REM sleep rebound.

The slow recovery in damaged brain processes help us to understand slow recovery of emotional balance. When for example Edinburgh medical students were faced with the anxiety of resulting final examination, bodily changes caused by this anxiety were gradual and slow over many weeks despite prompt knowledge of success at this examination. This suggests that the process of repair in anxiety are quite similar to the slow brain recovery following a drug insult. There is another element here also. Neurones that undergo active modification owing to involvement in the impact of emotional distress whether of physical or social origin, would recover differently in the normal than the abnormal individual.

It is not just deprivation of REM sleep that sets into operation protein synthetic machinery in the neurone, but deprivation of protein synthesis by such drugs as streptomycin. When the brain is immature there is a uniquely high proportion of REM sleep as occurs before and after birth in animals such as humans. During these months the finer differentiation of the brain occurs. There is also increased brain blood flow and temperature during REM sleep[4] findings consistent with the view that REM sleep is an external manifestation of active protein synthesis in the brain.

Sleep then consists of two types of restitution. Non REM which is enhanced after strenuous physical activity and REM sleep during which chiefly brain repair occurs.[5] If this be true then conditions associated with massive learning should cause high percentage of REM sleep as for example when an "enriched" environment leads to a heavier brain cortex and greater development of glial cells in growing rats.[6] In mental retardates, however, REM sleep is reduced both in amounts and intensity.

As we study brain and behavior we will increasingly be compelled to think in terms of slow shifts of function indicated by protein synthesis. Perhaps it is this mechanism which underlies personality modification through psychotherapy even as it underlies drug tolerance or REM sleep rebound. We know that the "healing of hurt minds proceeds by processes equally as slow as the healing of hurt brain cells".

L.H.N.

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Improving Cognitive Function In Senility By Hyperoxygenation

Cognitive functioning processes become impaired as one grows older. It has been shown that memory and learning peaks at an early age between 15-20 years.[1] It is also generally believed that imaginative creativity peaks at 25-35. It is likely that many people in functional stages between those of peak learning and gross senility are undergoing slow but progressive and measurable decreases in memory and learning function. Three explanations have been offered for this slow decline in cognitive functioning. One holds that we lose neurones at an accelerated

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rate as much as 10,000 per day and the accumulated loss leads to impaired cerebral functioning. Two explanations for this loss have been offered. One is the slow accumulation of mutations in nerve cells until some of them are unable to function effectively. These mutations cannot be thrown off because neurones do not reproduce as for example dermal cells and sperm cells do. Another holds that as oxygen delivery to neurons decline, their function is thereby impaired.

There are other possible causes for decline in functioning such as nutrilite deficiency of the nervous system. The prototype of this disorder is pernicious anemia in which the brain becomes deficient in vitamin B12 long before anemia becomes manifested. As far as is known an attempt to stem the progressive loss of neurones with aging has as yet not been studied. The slowing down of mutations is still theoretical. The syndromes of cerebral deficiency diseases are presently under investigation. The attempt to furnish oxygen in high concentration to the senile patient forms the basis of a study by Jacobs and his associates in a recent issue of the *New England Journal of Medicine.*[1]

Most studies relating oxygen supply to cognitive functioning have involved the effects of acutely induced hypoxia on the learned behavior of trained laboratory animals.[4] Results of such studies indicate that recent memory and learning are particularly sensitive to oxygen deprivation. There were no studies on the effect of increased arterial oxygen tension on cognitive function in senescent man until Jacobs study of 13 elderly males. He markedly elevated alveolar O_2 tension by administration of 100 percent O_2 in a hyperbaric chamber. When the group was breathing 100 percent O_2 they showed uniform and large increase in post exposure test scores. Those on low oxygen showed no significant improvement. The tested group showed large increases in arterial O_2 under hyperoxygenation while a control group showed no such increases.

We know that oxygen deprivation can impair cognitive function in general and memory storage for recent events. Thus the question arises whether some psychological symptoms of senescence arise from relative hypoxia of brain tissue. Oxygen delivery to any tissue depends upon arterial O_2 tension hemoglobin levels, blood flow, the state of the microcirculation and capillary tissue diffusion of O_2. All these factors may be impaired to some degree in the aged but no direct correlation has been established between such impairment and senility in man. Jacobs study indicates with a high degree of statistical significance that intermittent hyperoxygenation can materially improve psychological symptoms of senility for at least the period studied. It suggests some areas of the brain are marginally hypoxic in the senile patient and that high oxygen input favorably affects the oxygen delivery system at some point so that the function of this tissue is improved.

We know that O_2 storage is minimal and in fact it has been shown[5] that tissue O_2 tension may be expected to return to pre-exposed levels within 30 minutes of cessation of high O_2 breathing at this level. This period is probably much shorter for tissue with a high rate of O_2 extraction such as the brain. In Jacobs series however, the measured effects on functions is shown to outlast by far the increase in O_2 tension in fact by a factor of 24. This raises the question about the role of oxygenation and energy storage in cerebral metabolism, a fruitful area for future research.

Much remains to be learned about the practical value of hyperoxygenation in senility. For example will the treatment modify basic degenerative processes. The treatment, however, is the only form of therapy thus far which offers statistically significant improvement of function. There remains the question of how long the treatment should be carried out, the kind of a retreatment schedule necessary to maintain symptomatic benefit for any length of time. There is no physiologic basis for thinking that 2.5 atmosphere absolute of O_2 treatments twice a day for 90 minutes of exposure are in any way optimal. Higher tensions of 0_2 are probably unsafe, but perhaps lower tensions would have a similar effect. We must even learn whether this improvement in function can be achieved by the use of 100 percent O_2 at normal pressure.

The patients treated in this study were all suffering from severe deterioration of cognitive function which was essentially incapacitating and prevented them from caring for themselves. Jacobs work indicates only that the phychological symptoms of gross senility can be markedly and reliably alleviated by intermittent oxygenation and that the effects persist much longer than can be explained purely on the basis of elevated brain tissue oxygen tension. The

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authors used Wechsler's memory test scale, the Bender-Oestalt and Tien's Organic integrity scale and in each there was significant improvement after the high O_2 treatment. Further work in this area is potentially of great importance.

L.H.N.

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Genetic Factors, Serum Cholesterol And Cardiovascular Disease

It is known that cardiovascular disease often occurs in families.[1] The question not entirely answered is whether this is due to genetic predisposition or whether to environmental influences. Recent studies now make it probable that some people actually have a genetic predisposition to cardiovascular disease. Recent work has revealed a correlation between certain blood groups and concentrations of serum cholesterol. Two independent teams have found higher concentration of serum cholesterol in subjects of blood group A than in those of the other A B O groups. For example, Oliver[2] examined 6,000 healthy male donors and found mean serum cholesterol concentrations that were significantly higher when the blood group was A than when it was O or B. AB was exactly like A except that there were very few AB donors.

A survey carried out by Langman[3] in South Wales also showed that men with group A blood had a higher mean serum concentration of cholesterol. This same group in another survey took into account the Lewis blood groups. This study revealed that in 344 women the concentration of cholesterol in the serum was consistently higher in those with group A but found no correlation between the serum cholesterol and the ABO blood groups.

The Lewis group individuals with normal serum cholesterol were almost all "secretors" and sometimes have intestinal alkaline phosphatase in their serum which is particularly evident after a fatty meal. It seems then that the concentration of cholesterol in the serum is related to those genetic factors which are associated with the appearance of intestinal alkaline phosphatase in the serum. The line of reasoning runs like this. Intestinal alkaline phosphatase is a result of a genetic concentration. Increased intestinal alkaline phosphatase in the serum is related to increased cholesterol in the serum. Increased serum cholesterol increased the risk of cardiovascular disease. Therefore, genetic factors do play a role in some cases of cardiovascular disease.

The connection between intestinal functions and serum cholesterol in human beings is interesting in the light of knowledge that cholic acid and cholesterol in the diet can influence the synthesis of cholesterol in the liver in animals. Lynen and his group[4] have shown that bile acids are very effective inhibitors of cholesterol synthesis. When they fed rats on a semi-synthetic diet such animals synthesized much less liver cholesterol than rats that were fed a normal laboratory diet. If, however, the animals fed a semi-synthetic diet were also given a steroid that prevented the reabsorption of bile acids then such animals produced much more cholesterol. It indicates clearly that bile acids act to reduce cholesterol synthesis in the liver.

Lynen's work revealed a diurnal rhythm in cholesterol synthesis depending upon the synthesis of new enzymes. At all times, however, these investigators could cause a reduction of cholesterol synthesis by feeding the animals cholic acid. However, this experiment in no way affected the diurnal rhythm in cholesterol syntheses. This means that although the concentration of bile acids is not responsible for the diurnal variation, it can act as a powerful inhibitor of cholesterol synthesis.

This work suggests further study to compare the absorption of cholic acid and of cholesterol in human subjects to see if one affects the other.

L.H.N.

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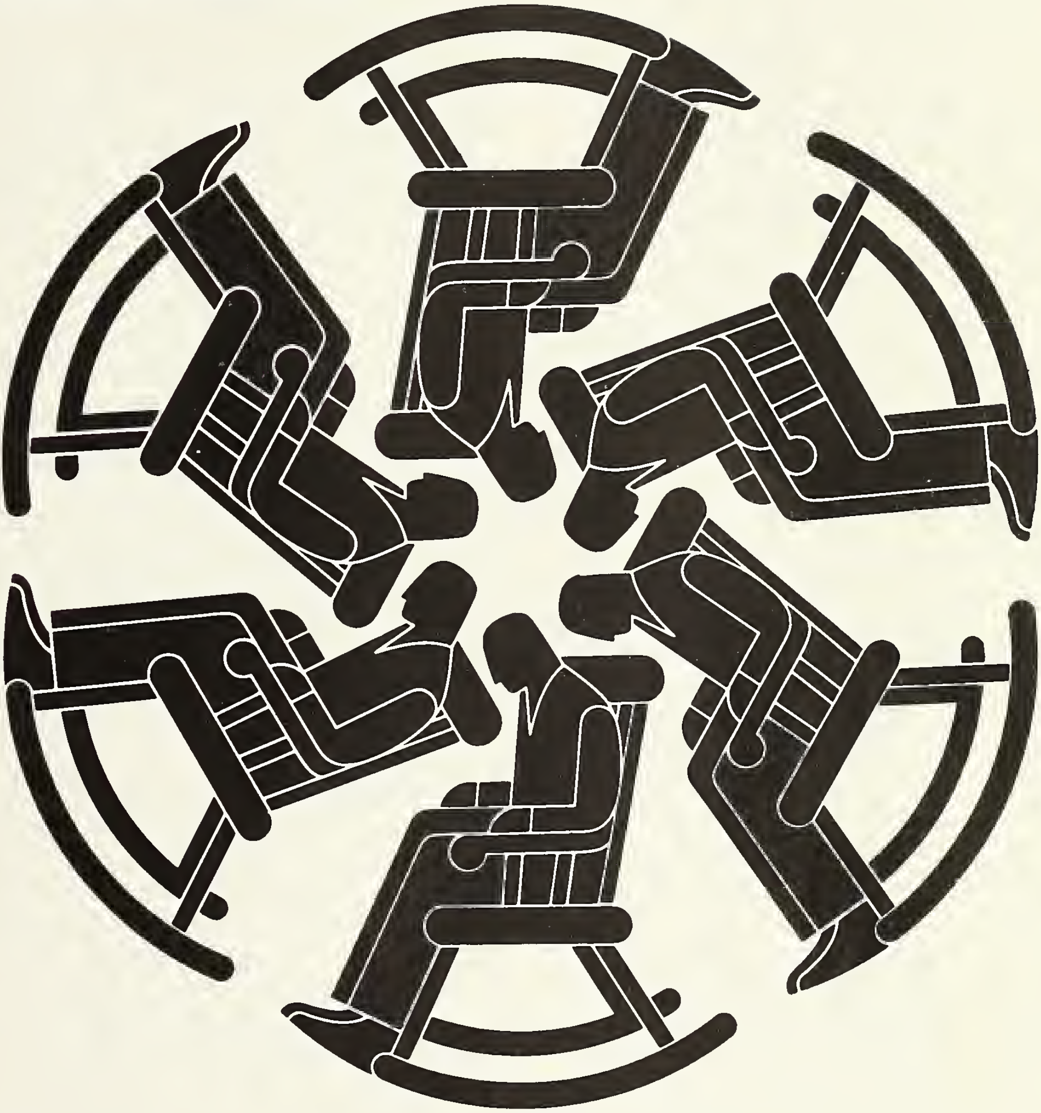

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What The Doctor Can Do In Solving The Problem Of Sudden Death

Green et al, described ten instances of sudden unexpected deaths which occurred in three generations. The average age of sudden death was twenty-one years. Eight of the ten had syncopal episodes preceding death. Minor variances were found in a detailed study of the cardiac conduction system. The authors theorized that a non sex-linked gene produced minor anatomical defects of the conduction system which ideally predisposed these individuals to the development of fatal arrthythmias triggered by a variety of environmental factors.

The scope of the problem of sudden death is much greater than is generally realized. Ten percent of deaths among the general population and forty percent among cardiovascular patients are sudden and unexpected as documented by Green, et al. The victims are by and large young (mean 45.1 years) productive with family and social dependents. Here then is a largely ignored area for significant clinical investigation to which the family physician can and must make vital contributions.

Sudden unexpected death is defined as occurring abruptly from non-accidental causes in a patient who had previously appeared to be in good health. Such an event is a catastrophe which affects the immediate family but also the physician and certainly the community as well. There are presently at least two basic approaches in the attempt to investigate this calamity. The first is to find out whether emergency resuscitation teams could reduce the mortality of sudden catastrophic events. Since death comes within four minutes after the cerebral circulation ceases, it is hardly likely that community-based cardiopulmonary resuscitation mobile units could save many lives.

The second approach is for the physician to search diligently for subclinical symptoms or signs that will identify the condition which could lead eventually to sudden death. The more common causes of sudden unexpected deaths are coronary artery disease, cardiovascular accidents, cardiomyopathies and cardiac conduction disturbances. Accordingly the first step in the investigation of sudden death is to obtain a complete and thorough autopsy examination. This will identify the majority of the disease states responsible for sudden death. Unfortunately when a patient is brought to the hospital DOA, the family must pay for the autopsy and many refuse to accept this expense in the face of the large problem of funeral and other financial burdens. This situation removes a large source of knowledge on this pressing problem.

If an autopsy is performed and no obvious reasons are apparent it is incumbent upon the physician in charge to obtain detailed pathological studies of the cardiac conduction systems all the way from the sinus node down to the distal ramifications. The next step, of course, is to obtain the compilation of a family history and appropriate investigations for the presence of preclinical manifestations of the disease states identified in the propositus. Studies such as these may help answer certain pertinent questions such as whether mobile community-based resuscitation teams with access to specialized care units can increase the salvage rate of sudden unexpected catastrophes.

Another question to be answered is whether early recognition and correction of carbohydrate or lipid derangements, obesity, hypertension, and other "risk" factors will affect mortality. Furthermore, can presently available drug therapy administered to young asymptomatic individuals with cardiomyopathies muscular subaortic stenosis prevent the disabling progression of the disorders and sudden death? How many individuals have unrecognized and potentially remedial extracranial cerebrovascular disease? Can recognition of familial conduction disturbances be treated and thus prevent fatal arrhythmias?

Such questions will be answered when we physicians fully recognize the big problem of sudden death and perhaps promote development of rapidly available cardiopulmonary resuscitation teams. We must especially identify the presence of a preclinical situation heralding the disease state and initiate appropriate investigative therapeutic trials.

L.H.N.

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Effect Of Alcohol On The Blood

Alcohol has been with us for an eternity. Knowledge of its effect upon the liver is very old and likewise upon the brain. Knowledge about its effect upon the lungs and heart is recent.[1] Now we are beginning to recognize another effect its action on the bone marrow. Anemia has often been noted in the clinical picture of chronic alcoholism. It has usually been attributed to the very poor diet of such addicts or perhaps to the cirrhosis of the liver which is often a complication.

A well confirmed observation is that when chronic alcoholics are admitted to a hospital and after alcohol is withdrawn and they are induced to take a hospital diet, then anemia soon remits. A reticulocytosis is followed by a rise in hemoglobin and if the white cells and platelet counts are low they too rise towards normal. This result could be due either to the alcohol withdrawal and or an adequate diet. The factor missing in a poor diet is generally held to be folic acid since this deficiency is marked by a change to megaloblastic erythropiesis with consequent macrocytic anemia. There may be other factors whose absence in the diet influences blood formation. It is scarcely possible, however, that alcohol itself could like chloramphenicol have a direct effect on blood formation so that the rate of production of new cells is slowed or fails to increase under the stimulus of anemia or infection.

To settle the question as to whether the recovery from anemia in the chronic alcoholic in the hospital was the effect of a good diet or the removal of a suppressive action of alcohol, Sullivan and Herbert[2] studied three patients who usually lived mainly on alcohol. One admitted that for six years she had taken ten "whiskey highballs" daily and that her diet rarely included meat, fruit or fresh vegetables. The patients were studied both on and off alcohol. They found that alcohol by itself can suppress the response of bone-marrow hemopoiesis to minimum doses of dietary folic acid, but that the depression can be overcome by giving large doses of oral folic acid or by stopping the alcohol.

Alcohol when given in the amounts used in these experiments caused suppression of formation of red cells, granulocytes and platelets and erythropoiesis was converted from normoblastic to megaloblastic in about ten days.

Another action of alcohol on the blood these authors studied was the known effect on serum iron levels and the saturation of iron binding capacity of the serum. They confirmed that ingestion of alcohol in their patients increased both these figures and when alcohol was withdrawn, the serum iron binding levels and the saturation of iron binding capacity of the serum again fell to normal. This action of alcohol on iron metabolism is quite separate from that in blood formation. It is known that suppression of erythropoiesis reduces utilization of absorbed iron, so that alcohol can be said to have a double effect on iron storage. When this is coupled with the well known effect on the often present liver dysfunction it must be very liable to increase iron stores in the tissues. Cirrhosis of the liver by itself does not often cause megaloblastic anemia with folate deficiency[3] and therefore the anemia of alcoholism is more attributable to the effects of alcohol rather than to liver disease.

Morphological changes in erythroblasts and other marrow cell has in fact been recorded in alcoholics. McCurdy, et al[4] drew attention to vacuolization in mormoblasts and myelocytes in the bone marrow smears of alcoholic patients which disappear when alcohol is withdrawn. Another abnormality of blood in alcoholics is the appearance of "ring sideroblats" that is erythroblasts that have iron staining granules in the cytoplasm arranged in a ring around the nucleus. Such patients have also folate magnesium and potassium deficiency in the serum. Such sideroblasts disappear in a few days once alcohol is stopped and a normal hospital diet is given. It appears that it is the folate deficiency that is the major factor in this disorder of the erythroblast.

All these results suggest that alcohol induces the abnormality of iron incorporation into haem that is thought to be represented by the ring sideroblasts only when folate is also deficient. Alcohol thus seems to be acting here in the same way as certain other toxic drugs are known to act, notably the antituberculous drugs and chloramphenicol. Pyridoxine also acts to reverse this toxic effect but the mechanism is at present unknown. What we must bear in mind is that disturbance in the normal formation of blood cells in the marrow must be added to the many effects of alcohol intoxication. The disturbance does, however seem to be limited to the chronic alcoholic who has replaced much of his food by alcohol and has been doing this for some years.

The amount of alcohol taken by and given to the patients investigated may beem to be well beyond social levels. But it is not too difficult if you are able to buy and consume one bottle of whiskey over a day's "nips" and it is surprising what a short time is needed to show definite changes in the bone marrow cells once dietary restriction has led to folate deficiency. The accumulation of increased iron in tissues and erythroblasts make it appear that "a rusty marrow" may follow close on the heels of a faulty liver in the alcoholic patient.

L.H.N.

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Horse Influenza And The Human Hong Kong Strain

The horse influenza virus A-equi/2 was isolated in 1963. In 1968 the Hong Kong variant of human type A2 influenza virus was also isolated. It soon became apparent that an antigenic relationship existed between these two types of influenza, that of horse and of man. It is only logical to consider then whether the Hong Kong variant was not actually the horse influenza virus or a very close relative. This idea required further analysis and also a test of the possibility of an exchange of viruses between species. Couch, et al,[1] carried out horse influenza virus challenge in human volunteers and reports the occurrence of clinical syndromes similar to those described for naturally occurring influenza. He produced the disease by inoculating antibody free volunteers with a strain of influenza A-equi/2.

The virus was obtained from a naturally infected horse and then passaged in human embryonic kidney tissue culture. It was then sprayed into the nose and nasopharynx of the volunteers. When the virus was first recovered in 1965 they gave it to six volunteers. The virus was recovered in feces but none of the subjects developed illness. In 1968 the work was repeated on fifteen volunteers. This time thirteen became ill with fever, rhinitis, headache, malaise, myalgia and weakness on the second or third day after inoculation. The most common response in eight was a febrile systemic and upper respiratory illness. Two others had lower respiratory tract involvement, cough substernal discomfort and tracheal tenderness. The illness was clearly indistinguishable from naturally occurring human influenza. The inoculated virus was recovered from all volunteers.

The first question to present itself is why the volunteers in 1965 developed no illness while most of those in 1968 did. One possibility is that the virus used in 1968 was more virulent because of the way it was stored and passaged. Perhaps also the environmental conditions were different since we know fall, winter and early spring are factors in making people more susceptible.

In spite of such questions the essential point made by Couch is important: that an inflluenza virus of equine origin produced a typical human influenza illness. This certainly supports the view that under natural conditions, equine influenza viruses may contribute to the emergence of new variants of human influenza. The results prove that exchange of viruses between species does occur.

L.H.N.

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Amniocentesis In Prediction Of Chromosomal And Behavioral Abnormalities

In a report to the Third International Conference on Congenital Malformation held in The Hague, Dr. Henry L. Nadler of Northwestern University Medical School described his results of amniocentesis on 150 women. It is now performed at the fourteenth week of pregnancy. At this time more than 90 per cent of the cells in the amniotic fluid can be grown in culture and thus provide sufficient material for diagnosing chromosomal and biochemical abnormalities. Earlier failure to achieve such accurate results was often due to obtaining anmiotic specimens too early in pregnancy.

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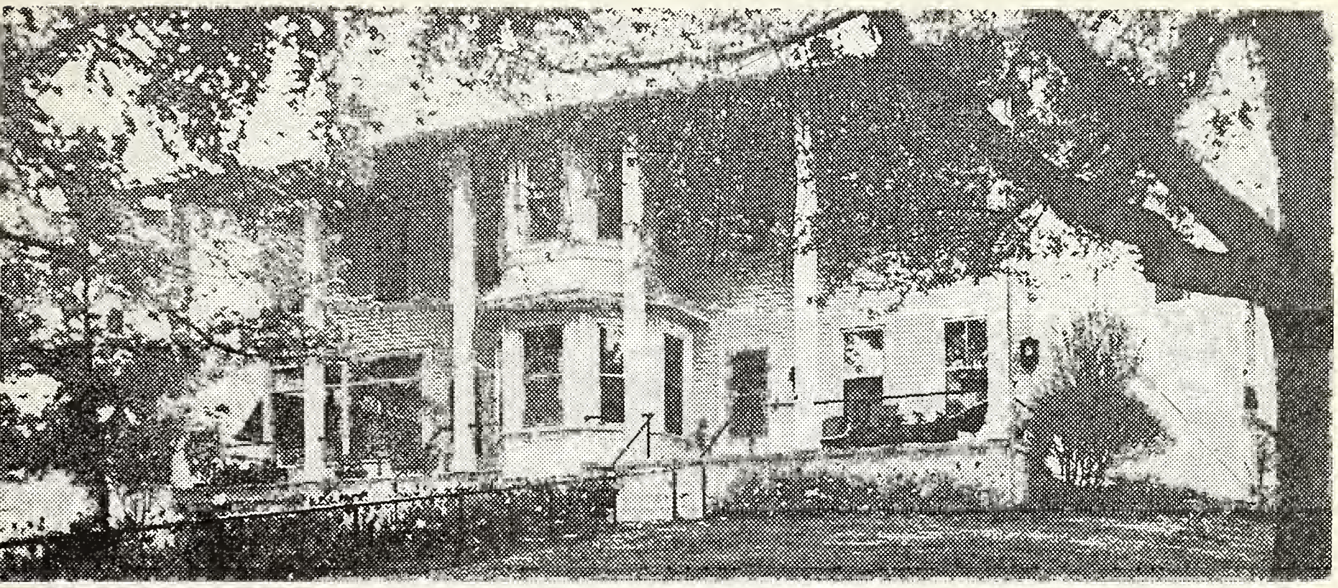

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During the three years of this study test results in fourteen patients clearly indicated chromosomal abnormalities. Thirteen of the women requested the termination of the pregnancy and in each case the abortus confirmed the accuracy of the test. The fourteenth pregnancy ended with delivery of a child with Down's syndrome (mongolism). All the remaining patients were given a normal prognosis and they all delivered healthy infants. This means that prenatal diagnosis of many congenital defects including chromosomal and biochemical abnormalities can now be made with 100 per cent accuracy. There were no false negative or false positive results.

The chromosomal pattern is studied in the epithelial cells presumably shed by the fetus into amniotic fluid. The cells are viable in 75 per cent of cases when obtained around the tenth week of gestation. Around the fourteenth week the samples are optimal. By the twenty-fifth week only one-quarter of the amniotic cells are still viable. Professor Nadler points out that amniocentesis is not indicated as a routine prenatal test. Rather it is an important procedure to be offered to women who may wish to consider termination of pregnancy if there is a clear indication of a life endangering defect in the fetus or of one known to carry the hazard of mental or physical abnormality.

There are a number of hereditary biochemical abnormalities which now can be detected by enzyme tests carried out on the amniotic fluid or on cultured amniotic cells. These include galactosemia, Pompe's disease, Marfan's syndrome and mucopolysaccharidoses. Such a procedure is particularly important in the case of galactosemia where there is a known family history of this disease or a previous pregnancy which resulted in an afflicted child. It is important to ascertain if any future embryo also lacks the enzyme necessary to metabolize galactose.

If a woman is known to have had a child with this disease, it is desirable to restrict her intake of galactose during pregnancy. Even so some of the sugar may reach the fetus and a number of children with galactosemia have been found with cataracts at birth. Furthermore, tests for galactosemia are not being done early enough or widely enough. About 20 per cent of babies with this disease go undetected and die early in life.

It is expected that the next decade will see an upsurge of interest in the technique of amniocentesis and that it will lead to treatment of some congenital aberrations. The possibility of correcting hormonal imbalance, of administering appropriate agents to loosen the meconium ileus plug in embryos otherwise slated for early death immediately comes to mind. So also can one imagine attempts at biochemical manipulation of enzyme defects. Such approaches are no longer as far-fetched as it seemed just a few years ago. Nadler's experience shows that for the present the thirteen mothers who elected termination of pregnancy were wise and the fourteenth who gave birth to a mongolian child was not so wise.

L.H.N.

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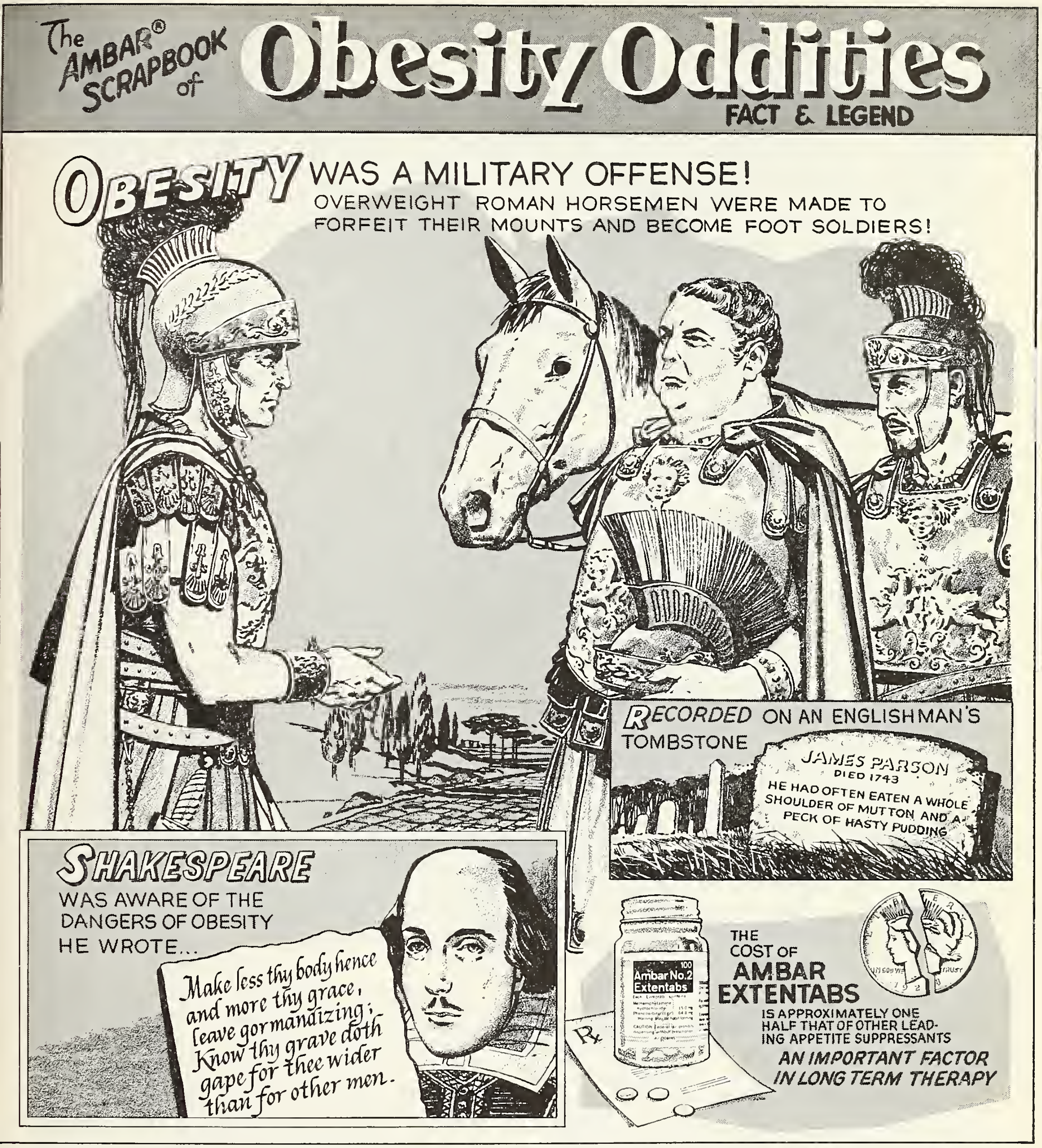
Education Of The Infant And Young Child

There is a forthcoming symposium in Boston on Education of the Infant and Young Child which is to review and summarize data which are now available at both human and sub-human levels concerning the effect of early experiences. Findings will be presented which demonstrate that the lack of appropriate experiences, or the occurrence of inappropriate ones will have deleterious consequences upon the growth, development and behavioral capabilities of the young organism. Other results will show that the performance capabilities of infants and young children may be significantly improved if one intervenes with the appropriate types of experiences in very early life. In addition there are data showing the need to continue these experiences if one wishes to insure the long-term positive consequences.

We have massive amounts of information from many diverse fields showing that the events occurring in very early life have long lasting and powerful impacts upon developing organisms including the human. We already know that the practice of feeding the infant on a schedule rather than on demand was bad practice. It caused hunger and emotional deprivation in the infant with deleterious consequences in the child. We know of the critical periods in behavioral development. There should be ways of utilizing this knowledge to develop maximum achievement in the growing child.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All these have generated trends in "early education" to start formal education at a much earlier age. At the present time there are a number of programs including day-care centers where very young children are exposed to a variety of educational experiences. Such centers are well advanced in Israel and many other countries. If one projects such a trend there will soon be day-care centers around the country which will be aimed at the very young child—six months old and particularly at that segment of the population which is often called "culturally deprived." A number of statements have already been made by various federal officials to the effect that day-care centers will be established as a means of taking care of infants and young children.

One question of great concern is, what experiences should these infants receive in day-care centers. The manipulation of experiences, educational, social and others in a day-care center offers the potential for great good, if we know what to do and great harm if we don't. Current data, sparse as they are, clearly establish that there is no one regimen or sequence of events which will optimally benefit all infants. A set of experiences which may facilitate a child's subsequent behavior along several pertinent dimensions may at the same time interfere with the development of other important behaviors. The degree and kinds of relationships between various types of experiences in early life and subsequent behavioral performance is not at present known. Professor Denenberg[1] points out that there is no adequate theory to guide those who have to make decisions concerning the kinds of experiences to give infants. This, therefore, is a matter of empirical determination in the day-care centers.

One of the points to be emphasized in the Boston Symposium is the extreme importance of having experimental day-care centers where various programs are evaluated over a period of years. The infant is our most important natural resource in the world today. He can assimilate and process information almost from the day he is born. He has capabilities for emotional reactivity and physiological involvement.

The growth and development of the infant into his adult capabilities are so important that they must no longer be ignored on the local and national level. It must become a subject of experimental investigation and effective evaluation. The day-care center is the logical place for such studies.

L.H.N.

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Case Histories In Environmental Degradation

At the end of World War II economic planners in Czechoslovakia decided to locate a large aluminum processing plant in Slovakia.[1] The military preferred a site in one of the narrow valleys of the Lower or Middle Tatra. Some scientists demurred on the ground that the smelter fumes would cause damage, but they had no hard facts to present and the plant was constructed in the valley.

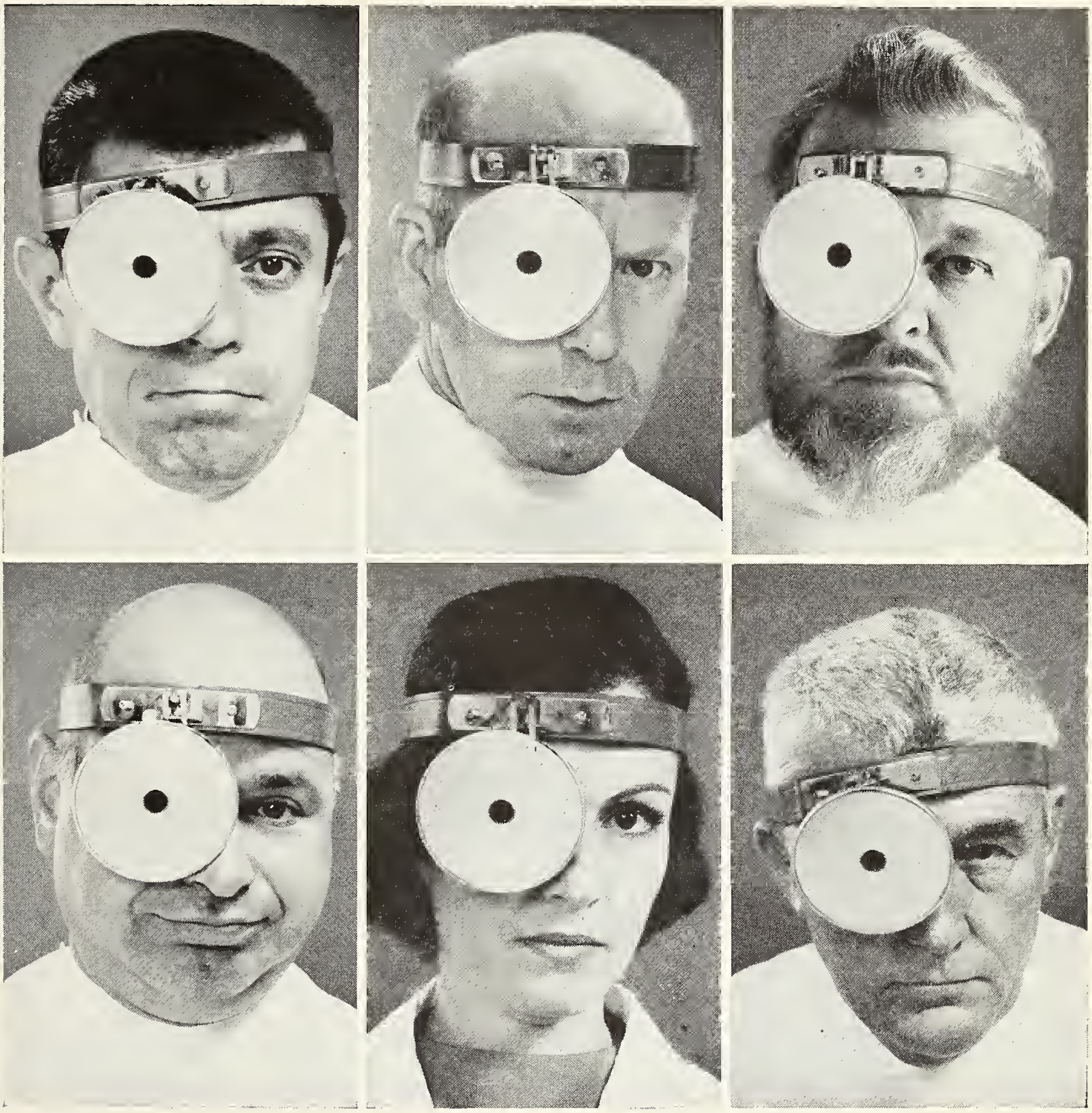
At that time the available fuel was the local coal high in sulphur content. Within a few months it became evident that the valley had a typical atmospheric inversion layer that trapped fumes in the valley. As the sulphur dioxide content of the air increased, all plants were killed and all animals that were not killed were driven away.

The mill workers had to live at a considerable distance, and at times they even had to wear gas masks in order to continue work. The result was an almost total industrial disaster that might have been foreseen.

This is only one example on a limited scale of the destruction that man today is visiting upon his environment. Many other examples were related at a conference held in December 1968 on the ecological aspects of international development.

A particularly glaring consequence of lack of foresight followed completion of the Aswan High Dam on the Nile. Clearly not included in the reckoning was the catastrophic effect upon the sardine fisheries of the eastern Mediterranean. Another effect of the Aswan Dam has been the rapid spread through the Egyptian population of infestation with parasitic blood flukes or shisto somiasis whose intermediate hosts are snails. The snails, of course, spread through the irrigation canals.

Finally there is the matter of the very brief life of the reservoirs impounding the irrigation waters. When a river carries a heavy burden of silt—like the Nile or Colorado or nearly all rivers in arid lands, the reservoir is filled with mud very



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quickly. What is to happen to the irrigation when the reservoir is filled?

Whether it be Nile, or Colorado or Mekong, every river system presents unique features. Each is a local system that is itself part of a wider system of interacting regions and successive times.[2]

The New York Academy of Sciences[3] has just published proceedings on pesticides which provides a comprehensive review of essential background information that all lovers of the land should read. The eight sections range from discussions of the general ecological aspects of pollution to the biochemistry, pharmacology and physiology of pesticides. Many of the classic pieces of work on the subject are described including the tale of the consequences of controlling gnats at Clear Lake, California. It will be especially valuable to supporters of the Environmental Defense Fund.

In September 1949, under strictly controlled conditions Clear Lake was treated with an analogue of DDT—DDD at a concentration of one part in 70 million. Biologists were persuaded that at this concentration the gnats would be destroyed but fish and birds would be unharmed. For two years no gnat larvae were found in the lake, but by September 1954 a second dose, this time one part in 50 million was needed and three years later a third dose at this concentration was applied.

In 1960, western grebes were found dying of tremors characteristic of poisoning by chlorinated hydrocarbons. The grebes contained up to 1,600 parts per million DDD. Moreover, there was a notable decline in the nesting population of grebes and the fish on which they fed contained even higher concentrations of DDD. Not everyone may be concerned at the fate of the grebes but the symposium describes an example of ecological disturbance with a direct effect on human health also.

In the Demerara River estuary in what was then British Guiana DDT was used in the forties to eradicate the mosquito Anopheles darlingi. By 1948, this vector of malaria had been eliminated, the agricultural economy of the area had been changed and mechanized crop farming had replaced animal farming. As a result A-aquasales which had previously fed on cattle began to feed off man and started to transmit malaria. During 1961-62 just ten years after the successful programs against A darlingi and malaria had finished, 93 cases of vivax malaria occurred in the Delta.

These issues multiplied by the hundreds for the sum of our technological alterations of the natural terrestrial environment explain why environmental scientists today speak with louder insistence of the need for a new approach to technological assessment. No piecemeal, limited approach can suffice. The biological, psychological and socio-cultural aspects as well as the engineering and physicochemical aspects need be introduced into the full analysis, and long-range economic aspects cannot be ignored in the prospect of immediate gain.[4]

L.H.N.

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Hazards Of Obesity

On October 19, 1968, the Obesity Association held a symposium at the Royal Society of Medicine in London on Medical and Scientific Aspects of Obesity.[1] No doubt was left in minds of the hearers that obesity is now a major public health problem and urgently requires medical and scientific attention. It was recognized by all that difficulties exist in defining the problem but conservative estimates put about half of the population above their "desirable" weight. "Desirable" meaning the relation between the weight of the individual and his physical status. Obviously, in a heart patient or hypertensive or diabetic we would choose a lower weight for our patients than if they were without physical impairment.

There is every indication that the incidence of obesity will continue to increase for childhood obesity is becoming more prevalent. J. K. Loyd pointed out that 80 per cent of obese children become obese adults. Experiments in patients who were already obese in adolescence when the body image appears to be developed reveal a galaxy of psychiatric traits that appear to be due to the obesity—obsessive concern with self image, passivity, expectation of rejection and progressive withdrawal which must be coped with if the patient is to become a happy well adjusted person. Many of these psychologic effects of

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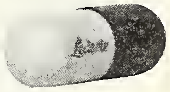

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obesity in childhood may tend to make obesity self-perpetuating and this is the reason why they are so difficult to handle adequately. In addition it was pointed out that the influence of intra-uterine and post-natal nutrition seems to be profound and could predispose the infant to obesity late in life.

In contrast to this J. T. Silverstone showed that obesity tends to be most prevalent among women over forty from the lower classes. In psychological terms these people who become obese, gradually, as they approach middle age usually adapt to this condition while they are becoming obese. At an earlier age, particularly adolescents tend to be vulnerable and become neurotic. For this reason there could be psychological risks attached to the treatment of these people for their obesity.

Until recently clinicians and many nutritionists believed that obesity was a result of gluttony and consequently the cure should be starvation. Professor KeKwick, however, warned that our knowledge of energy metabolism is not as complete as adherents of this point of view would suppose. This was amply demonstrated by D. S. Mills who provided substantial evidence for the ability of lean individuals to dispose of excess calories by increasing heat production, that is "thermogenesis." In view of this he proposed that a thermogenic defect could underlie the development of obesity and stated that a search had been started for thermogenic agents in the treatment of obesity.

This theme was taken up later by P. Turner. He started from a consideration of various drugs which suppress appetite and pointed out that some of them do have the additional property of stimulating peripheral metabolism. He suggested that an effort be made to develop this class of drugs because they are devoid of central stimulant activity. As far as dietary aids to slimming the low carbohydrate, high protein regimen was probably the most effective, practical and inexpensive. People who live on such a regimen eat a complete diet in all respects and if anything nutritionally better than their "normal" diet.[2]

The reduction of carbohydrates can lead to a considerable reduction in calories. In practice this kind of a diet would require no weighing, calculating or measuring other than avoidance of carbohydrate rich foods. On such a diet the proteins and fats will be found to regulate themselves, at levels that are no higher than in the ordinary diet. In fact one can ask his patient to eat as much as he likes of foods that contain little or no carbohydrates such as meats, fish, eggs, cheese, green vegetables, butter, cream, and one glass of milk if the carbohydrates are kept at about 50 grams. The results will be a diet in which calories are automatically restricted and the patient need never feel hungry. Professor Yudkin pointed out that such a diet is nutritionally sound and cannot lead to deficiency of some nutrients.

The obesity problem is complex.[3] Difficulties in obtaining recognition of obesity as a major health hazard are considerable. Without doubt research into this problem will be accelerated by such organizations as the Obesity Association. How to deal with the obese person, to increase his physical activity, to recognize the psychologic aspects, motivation and thermogenesis remains the great challenge.

L.H.N.

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1. Gordon, E.E. and Haas, A., Industr. Med. Surg. 28:217, May, 1959.

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Fetal Intrauterine Transfusion II — Review of Indications and Management

Maclyn E. Wade, M.D., John A. Ogden, M.D., and Clarence D. Davis, M.D.

Fetal intrauterine transfusion (IUT) for the management of Erythroblastosis fetalis was first introduced by Liley in 1963[1]. Transfusion was based upon the concept that mature erythrocytes infused into the fetal peritoneal cavity would be rapidly absorbed by the lymphatics and enter the fetal circulation intact.

Since the initial reports of the use of IUT at Yale in 1966[2, 3], over two hundred women have been subjected to spectrophotometric analysis of their amniotic fluid. Based upon the results of spectrophotometry, fifty-nine of these patients have undergone a total of one hundred and twenty-five intrauterine transfusions.

The experience gained from this patient population has necessitated a presentation of the current techniques, a review of the results and a reevaluation of the criteria for IUT

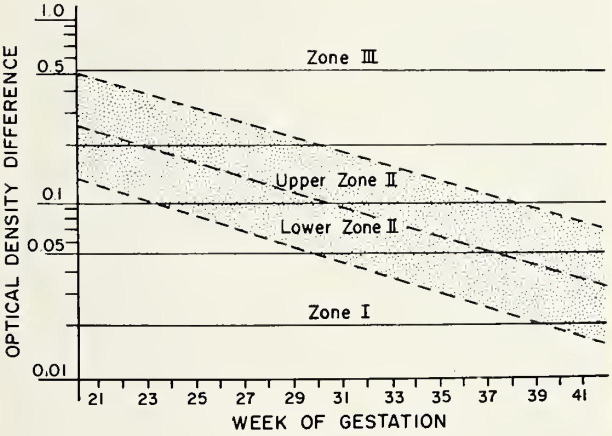

Figure 1

Modified from Liley. Zone I—Fetus mildly affected or unaffected. Zone II—Fetus mildly affected or unaffected. Zone III—Fetus severely affected.

Materials and Methods

Patients were considered candidates for initial amniocentesis if they had a positive Coombs titer of 1:8 or greater in the current or previous pregnancy, or if they had previously given birth to an Rh-sensitized baby. Whenever possible the initial amniocentesis was performed at twenty weeks of gestation. Subsequent specimens were obtained contingent upon the patient's degree of sensitization. In interpreting the spectrophotometric results (specific optical density difference at 450 millimicrons—ΔOD), we preferred to consider any optical density difference that rose rapidly toward Zone III (Figure 1) indicative of significant potential risk to the fetus. Thus, any pregnancy of less than thirty-two weeks gestation exhibiting an amniotic fluid optical density difference in the upper quarter of Zone II or Zone III was immediately considered a candidate.

Three types of transfusion techniques were evolved, only one of which has proved satisfactory. One technique for helping small fetuses of less than 25 weeks gestation was hysterotomy and direct implantation of the catheter into the fetal peritoneal cavity (Figure 2). The fetus was then replaced in the uterus and the membranes and uterus closed.

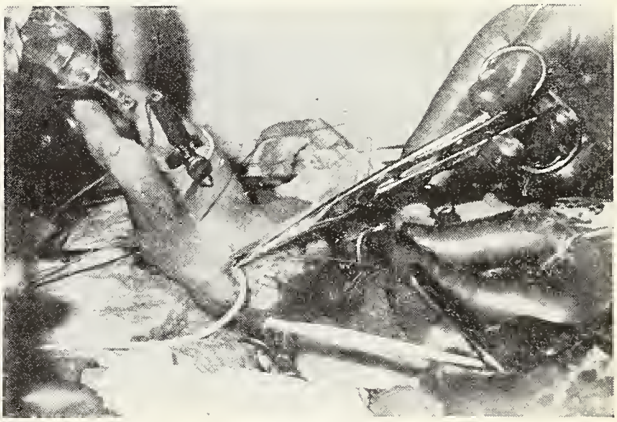

Figure 2

Silastic catheter, inserted into fetal peritoneal cavity, being transfixed to abdominal wall. Electrode on left leg of fetus to permit monitoring of fetal heart rate.

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This was done in three patients, with no survivals. The low fetal survival combined with the potentially high risk of morbidity led us to discontinue it. A second technique was transabdominal amnioscopy using a modified pediatric fiberoptic cystoscope (Figure 3). The purpose was to allow direct placement of the transfusion needle in the lower quadrants of the fetal abdomen under direct visualization. The procedure was successfully completed in two patients, but only one fetus survived. The risk of rupture of the fetal membranes was considered significant and prompted us to discard this method.

The third, and most frequently used, procedure was a needle technique utilizing fluoroscopic image intensification. Approximately thirty minutes prior to the initial transfusion 30 ml. of amniotic fluid was withdrawn and replaced by an equal amount of 50% sodium diatrizoate*. This contrast media was frequently swallowed by the fetus and concentrated in the fetal gastrointestinal tract. Preliminary films, using a wire abdominal grid, were then taken to ascertain the location of the fetal abdominal cavity (Figure 4). Using fluoroscopic image intensification and videotaping a 7 inch 17 gauge Touhey needle was directed into the lower half of the fetal peritoneal cavity. A small injection of Hypaque was used to ascertain the location of the transfusion needle. Any needle in the fetal musculature was left in place for stabilization, and further needle placement was undertaken. The transfusion was performed with fresh, Rh-negative, maternally compatible erythrocytes that had been washed twice with saline to remove the buffy coat and then packed to a hematocrit of 90 per cent. The blood was injected unwarmed through a three-way stopcock into the fetal abdomen at the rate of 5 ml. per minute. The amount of blood used is shown in Table 1. Once the initial transfusion had been carried out, succeeding transfusions were performed every 10-21 days until the fetus was felt to be large enough to survive induction and extrauterine life (usually 34-36 weeks of gestation).

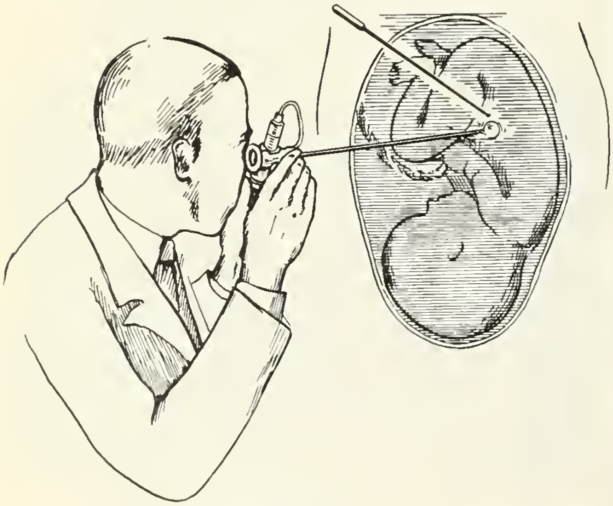

Figure 3
Artists rendition of Amnioscope in operation—Note: Air inflated balloon permitting needle to be inserted into fetal peritoneal cavity under direct visualization.

TABLE 1

AMOUNT OF IUT

Week of Gestation	*Instilled Erythrocytes* (ml.)*
20-23	35
24-25	45
26-27	55
28-29	65
30	75
31	85
32+	95-105

* Erythrocytes packed to hematocrit of 90% before measuring amount of infusion.

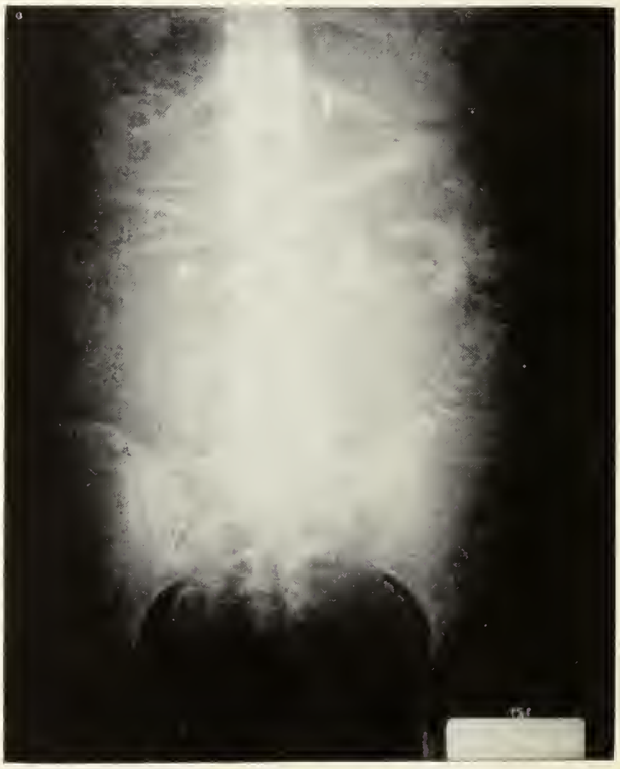

Figure 4
Arrow points to contrast media inside fetal intestine. Thin lines are from the wires of the grid placed over the maternal abdomen.

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* Hypaque—Winthrop Laboratories

TABLE 2

SUMMARY OF RESULTS OF FETUSES BORN ALIVE FOLLOWING IUT

No. of Transfusions	*No. of Pts.*	*Aver. Cord Hgb.*	*Aver. % Fetal Hgb*	*Neonatal Death*	*Living & Well*
5	3	10.0	7.5	1	2
4	5	14.8	4.1	0	5
3	5	14.8	19.3	2	3
2	9	13.9	27.2	4	5
1	9	9.2	50.5	3	5
Total	31			10	21

Results

Using the aforementioned techniques 125 transfusions were performed in 59 patients. There were 28 in utero deaths (47.5%). Table 2 presents a composite summary of those fetuses born alive. Thirty-one patients were born alive following one to five intrauterine transfusions. Ten died in the neonatal period (16.9%), while twenty-one are alive and well (35.6%). Seven of the eight fetuses requiring four or more transfusions in utero have survived beyond the neonatal period. The average fetal hemoglobin percentage in these patients was much less than that of those fetuses receiving one to three intrauterine transfusions. Further, those fetuses with tht greater number of intrauterine transfusions required fewer neonatal exchange transfusions. The two survivors who received 5 IUTs are the only two reported in the literature[4].

Table 3 correlates the absolute survival with the week of gestation of the first intrauterine transfusion. The survival was directly proportional to the gestational age. Only 15% of the fetuses transfused initially during the gestational ages of 20 to 24 weeks survived, whereas amost 75% of those transfused after 29 weeks survived.

The aforementioned survival figures were influenced by the presence of fetal ascites at the time of initial IUT (Table 4). Seventeen fetuses were ascitic at the time of initial transfusion, with only one (5.9%) surviving. In contrast, 42 were non-ascitic, of whom 20 (47.6%) survived. If these figures are further analyzed according to the week of gestation, the influence of ascites is further manifest. The presence of ascites prior to twenty-nine weeks was not associated with any survivors, while the absence of ascites prior to twenty-nine weeks led to ten survivors (37%). If the initial IUT was performed after thirty weeks, there was one survival (1/3) in the ascitic group and ten survivors (10/12) in the non-ascitic group.

TABLE 3

ABSOLUTE SURVIVAL RELATED TO INITIAL IUT

Week of Gestation of First IUT	*No. of Pts.*	*Survivors*	*% Survival*
20-24	19	3	15.7
25-29	25	7	28.0
30+	15	11	73.2

TABLE 4

RELATION OF FETAL ASCITES TO PERINATAL SURVIVAL

	Ascitic Fetuses				*Non-Ascitic Fetuses*			
Week of Initial IUT	*T*	*S*	*ND*	*L*	*T*	*S*	*ND*	*L*
20-24	4	4	0	0	12	9	3	3
25-29	10	6	4	0	15	6	2	7
30+	3	1	1	1	12	2	0	10
Totals	17	11	5	1	42	17	5	20

T—Total
S—Stillborn
ND—Neonatal Death
L—Living & Well

Comment

Based upon the analysis of the data in this series, we feel that the criteria for intrauterine transfusion previously presented[5] should be revised.

If the estimated gestational age is between 20 and 24 weeks, the fetus should be transfused if serial optical density difference values rapidly rise into the upper quarter of Zone II or into Zone III. Further, two separate ΔOD determinations in Zone III indicate the necessity for immediate transfusion. If the fetus exhibits hydrops or a significant amount of ascites or if the viability of the fetus is in doubt, no transfusion should be undertaken.

Between 25 and 32 weeks of gestation, the same OD criteria should be used. Even at 32 weeks if the age of the fetus appears less than the estimated gestational age, the patient should be transfused rather than induced.

Certain general indications should also be considered. If the patient is clinically leaking amniotic fluid vaginally, is not in labor and has a fetus of less than 32 weeks gestation but felt to be viable, transfusion should be instituted in an effort to obviate possible intrauterine death, premature induction, respiratory distress syndrome or multiple neonatal exchange transfusions.

Once the transfusion procedures are initiated, subsequent transfusions should be performed at 10-21 day intervals until the fetus is approximately

36 weeks gestational age and clinically appears capable of survival. Following the initial transfusion, serial ΔOD values should be considered helpful only if they clearly demonstrate a marked increase or decrease. The necessity of further transfusion should not be contingent upon these values.

Summary

1. The results of 125 fetal intrauterine transfusions in 59 patients performed at the Yale-New Haven Medical Center are described.

2. The revised criteria for the selection of patients for intrauterine transfusion are presented.

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Recognition of Pulmonary Embolism and Infarction

From the experimental and clinical information at hand, it is apparent that a multiplicity of physiologic events is set into operation by pulmonary embolism, and its possible sequel, infarction. Therefore, it is not surprising that the resultant array of symptoms may overlap with those of other cardiac and pulmonary disorders, so that the clinical differentiation often becomes difficult. As a matter of fact, it has been reported that, of cases of pulmonary embolism at autopsy, the correct diagnosis had been made in only 20 to 50 per cent of the patients during life. . . . The two diseases for which pulmonary infarction is most frequently mistaken are pneumonia and myocardial infarction. . . . Certain cases of congestive heart failure, and other forms of pulmonary disease (especially atelectasis, pleurisy, pneumothorax, pulmonary neoplasm, and infection such as tuberculosis) are often manifested by very similar symptom complexes. . . . In addition, primary pulmonary artery thrombosis is occasionally indistinguishable from pulmonary embolism. This uncommon disease process may cause such extensive thrombotic occlusion of the pulmonary arteries as to incite intractable right heart failure with severe dyspnea or to resemble acute massive embolism. . . .

It has been difficult to establish accurate estimates of the mortality rate of patients with thromboembolism of the lung because the clinical diagnosis is frequently obscure. Barker and his associates . . . found a death rate of 38 per cent in a study of 879 cases. Macleod and Grant . . . and Byrne . . . reported a mortality of approximately 20 per cent, the latter study comprising more than 700 instances of embolic accidents to the lungs. Of the patients who died, Byrne noted that 84 per cent succumbed with the first episode. Wolff . . . has emphasized that the likelihood of fatality is increased with succeeding embolic attacks. The immediate cause of death is usually related to acute circulatory collapse or from overwhelming strain and failure of the right ventricle due to pulmonary arterial occlusion. . . . Many patients become comatose preceding death. . . . In patients who survive the acute effects of the embolic process, the general prognosis is related to the underlying disease . . . and particularly to the form and severity of existing heart disease.—Parker, B. M., and Smith, J. R.: Pulmonary Embolism and Infarction: A Review of the Physiologic Consequences of Pulmonary Arterial Obstruction, *Amer J Med* 24:402-427 (March) 1958.

Ocular (Pigmentary) Effects of Psychotropic Drugs

William S. Appleton, M.D., Richard I. Shader, M.D. and Alberto DiMascio, Ph.D.

Concern about the effects of psychoactive drugs on the eye has increased sharply since Greiner[1] and Siddall[2] reported depositions of pigment in the lens and cornea in 1964 in patients receiving chlorpromazine. A previous peak in interest had occurred in 1959 when Kinross-Wright[3] demonstrated thioridazine-induced pigmentary retinopathy. Such side reactions are associated with organic changes in the eye and are thus much more alarming than the annoying but more common blurring of vision or the less frequent, but still not serious oculogyric crises. Physicians using these agents must learn how to recognize and treat such complications and how to prevent their occurrence. In this paper we review the complications of psychotropic drugs which are associated with pigmentation. A subsequent report[4] will cover blurred vision and glaucoma as they relate to the autonomic effects of psychotropic drugs.

Cornea and Lens

In 1956, Goldman[5] noted skin pigmentation apparently caused by chlorpromazine. However, it was not until 1964 that the syndrome of skin and eye pigmentation changes was observed by Greiner[1] and then by Siddall[2]. Many authors have since described this phenomenon· Siddall writes of these lens and cornea changes as follows: ". . . a light dustry pigment . . . appears on the lens capsule . . ., eventually (taking) the form of (a) stellate cataract, whose early stage may a very dim outline· Eventually a polar cataract change will be noted in the anterior part of the lens, and by this time the brown pigmentary change seems to have faded considerably. The early stellate form which has a rather brownish outline to begin with, also becomes very light in color. The lens changes seem to be limited to the anterior part of the lens. The anterior lens pigment is regressive ,while the stellate and polar cataracts are not[6]." There has been great variation in the reported incidence of these ocular conditions. DeLong[7] reports 15% while Siddall[2] has reported 74%. Such discrepancy is due to differences in dosage, climate, patient sample and ophthalmologists' criteria for defining pathological conditions. DeLong[7] advocates more careful distinction between chlorpromazine-induced changes and a lens abnormality which he calls "axial punctate opacities". The latter occurs in 6-10% of the general population, especially in people over 40 years old. Although similar in appearance to drug-induced opacities, these formations are smaller, darker ,and more clearly defined than the early stages of chlorpomazine-induced changes. Such distinction requires careful ocular examination before drug therapy is initiated. Some clinicians have attempted to distinguish between this and similar "non drug-related" ocular changes by only considering cornea and lens changes of a defined severity. Such an attempt has been made by Forrest and Snow[8] who graded ocular deposits from 1+ to 5+.

The difficulties in differentiating drug induced from other causes of corneal and lens opacities were noted by Prien and Cole[9], who found that as their large-scale study continued, the participating ophthalmologists changed their minds about what they had originally observed in the cornea and lens. They became unsure of their original baselines. This and DeLong's comments[7] suggest that the reported incidence of corneal and lens opacities is influenced by the examining ophthalmologist's familiarity with this entity.

There is general agreement that pigmentation occurs in the following sequence: anterior lens, posterior cornea, anterior cornea, conjunctiva, skin and finally, the retina[2, 10, 11]. If pigmentation is present in the skin, it almost certainly is associated with deposition in the eye and is therefore suf-

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ficient justification for a thorough eye examination. Although the subject of skin pigmentation has been reviewed elsewhere[12], it is important to stress its association with eye disorders.

The cornea and lens ought to be examined by pen-light or ophthalmoscope in order to observe these changes. Such examination should be made prior to any chlorpromazine and at subsequent intervals—varying with dose level. On large doses (e.g., 1,000 mg. of chlorpromazine or its equivalent for two years) Forrest and Snow[8] recommend examination every three months; on smaller doses, once a year should suffice.

Investigators differ about whether these corneal and lens particle depositions are reversible. Soulairac[13], Barsa[14] and others believe them irreversible. Others such as Siddall[6], Greiner[15], Forrest and Snow[8], and Mathalone[16] consider the changes to be at least partially reversible.

Strenuous effort to eliminate corneal and lens deposits have been made by Greiner *et al*[17]. These investigators have tried a number of techniques for reducing coloration in several groups of patients with abnormal pigmentation due to chlorpromazine· They seem to have achieved substantial improvement of skin pigmentation and moderate-to-questionable improvement of ocular pigmentation by:

1) administering D-penicillamine as a chelating agent;
2) by secluding the subject from direct sunlight;
3) by keeping the subjects on a low-copper diet; or
4) by injection of melatonin.

Forrest and Snow[8] report that substituting perphenazine, trifluoperazine, or fluphenazine for chlorpromazine can maintain psychic improvement while arresting ocular and dermal pigmentation. Butyrophenones or thiaxanthenes could also be substituted.

Chlorpromazine-induced lens changes result from an accumulation of deposits the nature of which has not been defined[7]. These findings should not be called cataracts because they are depositions rather than losses of lens tissue transparency. Szabo[18] suggests that the excess pigment is melanin, while Barsa *et al*[14] have suggested that the condition results from some other alteration of the chemistry of the aqueous humor. The melanin hypothesis attempts to explain why skin and eye pigment is intensified by sunlight[6] and seems more prevalent among individuals with dark skin, hair, and eyes[13].

Investigators agree that corneal and lens deposits do not interfere with visual acuity, until they reach a very advanced stage. If it is true that they can progress to pigmentary retinopathy, then they ought to be treated early to forestall this more serious complication. Corneal and lens opacities have been definitely associated with only a few phenothiazines, and many believe that only chlorpromazine is responsible. However, Siddall[6] also points to thioridazine, and Margolis and Goble[19] urge caution with all phenothiazines.

The occurrence of corneal and lens opacities due to prolonged phenothiazine administration is definitely a dose-related phenomenon· The deposits seem to result from the accumulation and retention of a chlorpromazine-melanin complex in the eye tissue[20] and may be formed even after drug treatment has been stopped. Total drug ingestion of 1,000 gm or more is associated with most of these ocular changes, but some investigators have reported cases at lower total dosage (Forrest and Snow, for example, at 750 gm[8], Barnes[21] at 550 gm). While dose-related, however, these conditions also seem to be idiosyncratic, since not all the patients on even the highest dosage levels have developed excessive pigmentation.

Epithelial Keratopathy

Another ocular side effect which seems to be similar both in cause and mechanism is epithelial keratopathy as reported by Johnson and Buffaloe[22]. This condition is characterized by white, gray and brown opacities of linear, curvalinear or spiral formation. These opacities are confined to the portions of the cornea ordinarily exposed to the light. Johnson and Buffaloe observed this condition in roughly two-thirds of a group of thirty chronic schizophrenic patients who were receiving 2,000 mg/day or more of chlorpromazine. They reported that the epithelial keratopathy "appears to differ from the lenticular, deep corneal and conjunctival changes associated with chlorpromazine in that it is related to high daily dosage rather than total dosage"[22]. In some cases the total dosage ingested was less than 550 gm of chlorpromazine. Only six of the 19 patients with epithelial keratopathy also showed the chlorpromazine-associated corneal and lenticular changes discussed above. Researching the hypothesis that these opacities had been deposited by tears, an analysis of tear fluid from the affected individuals was made. This disclosed that chlorpromazine-like compounds were indeed present in the tears; however, because of the small quantities involved, the results were not conclusive.

Pigmentary Retinopathy

Pigmentary retinopathy has been defined by Potts as ". . . either clumping or rarefaction of pigment; decreased visual acuity, which usually improves markedly on cessation of the drug; marked slowing of dark adaptation, and during the acute phase, extinction of the electroretinogram"[20]. Kalinowski outlines the fundoscopic appearance of this condition as "pigment deposits spreading from the middle zone between the equator and posterior pole anteriorily and posteriorly. . . . Over a period of three to four weeks, the pigment coalesced into larger sheets and edema appeared which persisted for five to eight weeks"[23]. Before these changes are apparent to the examiner, however, the patient may be aware of a brownish discoloration of vision, usually occurring between the 20th and 50th day of treatment with drugs[23].

Although Potts states that chlorpromazine may produce such retinal pigmentation (or depigmentation) secondarily, this condition is principally caused by thioridazine. The retinal changes occur after large doses of thioridazine (over 1,200 mg. daily) and often appear within a relativtly short period of time, usually on the order of four to eight weeks[16, 24]. The relationship appears to be a function of time and dose, rather than simply from dose accumulation.

Thioridazine administered at levels up to 800 mg daily seems to be "safe." We are not aware of reports of significant complications in cornea, lens or retina at or below this level. Some investigators have recommended thioridazine in moderate amounts as a substitute for chlorpromazine especially in patients in whom chlorpromazine has produced corneal and lenticular opacities[8].

When thioridazine does cause retinal pigmentation, a drastic reduction in visual acuity or even blindness may result[25]. Generally, investigators believe retinal pigment deposition is irreversible[26]. Treatment attempts, similar to those used to induce cornea and lens depigmentation in chlorpromazine-associated cases, have not resulted in any clear improvement of retinal pigmentation associated with thioridazine[17]. However, visual acuity usually returns when the thioridazine is discontinued. Other antipsychotic agents may be substituted.

These deposits of pigment can only be detected by the ophthalmoscope. Patients should be given a complete ocular examination *before* drug therapy is initiated, and those receiving large doses of thioridazine should be examined by fundoscope monthly for the first few months of treatment. Since chlorpromazine-induced retinal pigmentation can occur in association with advanced cornea and lens changes[24], the retina should also be carefully examined when corneal and lens deposits exist. Finally, any patient reporting a brownish discoloration of vision, or decreased dark adaptation, should be examined in order to disclose and possibly prevent pigmentary retinopathy.

Frequency of Eye Side Effects

In 1966 twenty-seven of the longest-term, highest-dose phenothiazine patients at the Massachusetts Mental Health Center were studied[27]. Each patient was seen separately by each of two ophthalmologists, who recorded his findings before consulting the other. Ten of the twenty-seven patients (37%) were found to have lesions worthy of comment—five were of the fundus, and five were confined to cornea and lens. Of the latter five, there was one definite "fine white powder located on the anterior lens" in a patient who had received 912 gm of chlorpromazine. The other lens deposit was of questionable nature. The three other cosnea and lens findings included: a "typical congenital pupillary membrane remnant," a "fine silky set of lines in the specular shagreen reflection of doubtful significance," and "fine peripheral radial lines of pigment on anterior surface of both lenses, believed to be congenital persistant strands." It seems reasonable to state, that the decision to report an incidence of 5/14 or one of 1/14 (14 is the number of patients on chlorpromazine) was a function of the judgement of these two opthalmologists. The caution of these observers meant a recording of 7.2% incidence of cornea and lens pigmentation in our high-dose, long term series, rather than 35.7% (5/14). Other factors important in explaining the variation in incidence of reported side effects in other studies include dosage, patient sample and climate (in photosensitivity reactions).

Seriousness, Reversibility, and Prevention

Commenting in order on each of the subjects discussed in this review one can begin by saying that blurred vision is not serious, except in cases of glaucoma. It reverses by itself either after a short period of time or after dosage reduction, and it can be prevented or minimized by using low doses and by not giving antiparkinsonian agents of the anticholinergic type prophylactically. Cornea and lens pigmentation are irreversible or at best only partially reversible. However, they are not serious in their effects on visual acuity except in very far advanced cases. Such deposits in cornea and lens can be prevented by low dosage, by drug holidays (every other day, or weekends) and perhaps by combination of chlorpromazine, which at present seems the main offender, with other phenothiazines during long-term maintenance. Thioridazine-induced retinopathy is associated with decreased visual acuity and even blindness, Visual acuity can improve rapidly when the drug is stopped, even though the pigment is not completely reabsorbed. This condition can be prevented by using thioridazine in daily doses less than 800 mg. Physicians should conduct ophthalmoscopic examinations at regular intervals in patients on long-term or high-dose phenothiazine regimens and should be attentive to such patients' complaints about visual difficulties.

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The Effect of Thyroid Therapy on The Hyponatremia and Hypoosmolality of Myxedema

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Introduction

Recently the lack of thyroid hormone has been mentioned as one cause, among many, of the inappropriate secretion of antidiuretic hormone[1-3]. A case is presented which provides added evidence for the role of thyroid hormone influencing antidiuretic hormone secretion.

M.H., a 68 year old female was admitted to the Hospital of St. Raphael on January 2, 1968, because of confusion and disorientation. Past history revealed the clinical onset of diabetes mellitus in 1952 with subsequent blindness. Her diabetes was recently controlled on acetohexamide 500mgm. daily. For three days prior to admission she was noted by her family to be fatigued and eating poorly. These symptoms progressed to lethargy and finally disorientation which prompted her admission. She had taken no other medication other than the acetohexamide which she took on the day prior to admission. A blood sugar drawn in the Emergency Room was 26mgm%. At that time a diagnosis of acetohexamide induced hypoglycemia was made and the patient responded dramatically to intravenous glucose. Physical examination disclosed an obese, somnolent woman with a low husky voice. Her mentation and vocal response were slowed. Blood pressure was 140/80, the pulse 76, rectal temperature of 96°F, and respirations 16. She had a puffy face, especially in the periorbital areas. Both eyes were aphakic, the skin was cool and not thickened, neck veins were not distended and no thyroid tissue was palpable. Cardiac examination revealed a grade I/VI soft blowing apical systolic murmur and the lungs were clear. Abdominal examination was normal. The deep tendon reflexes showed a markedly delayed relaxation phase. Our first impression was myxedema.

Initial laboratory studies showed a hemoglobin of 12.9 grams per 100ml., hematocrit of 38%, white cell count of 12,500 with a normal differential. Urinalysis revealed a trace of glucose, no albumin, a S.G. of 1.015 and a pH of 5.0. The sediment was normal. Following admission the blood sugar was 120mgm%. It remained in this range during the remainder of her hospital stay. Initial blood urea nitrogen was 55mgm% and promptly fell to 16mgm% after hydration. The serum creatinine was 0.9mgm%. Admission electrolytes were sodium 140, chloride 94, bicarbonate 31.2, and potassium 3.1mEq/liter. Chest x-ray was normal and an electrocardiogram revealed low voltage and a first degree A-V block. Further studies: The serum protein electrophoresis was normal. PBI was 0.8 micrograms. 24-hour I^{131} radioiodine thyroid uptake was 2%; Following three days of 10 units daily of intramuscular thyrotropin it rose to only 6% in 24-hours. Serum cholesterol was 460mgm%. Serum cortisol 29mcg%. 24-hour urinary 17-hydroxy and 17-keto steroids were 1.6 and 4.0mgm, respectively. 24-hour urinary follicle-stimulating hormone was positive at 6.5 and negative at 13 mouse units. Skull films showed no abnormality of the sella turcica.

Hospital Course: Despite adequate fluid intake and a ten gram sodium chloride diet the plasma sodium declined gradually and dropped to a low of 114mEq/liter. On that day the serum osmolality was 247 milliosmoles/liter and a simultaneous urine osmolality was 391. The urine for sodium was inadvertently discarded. Because of the patient's poor clinical condition she received 350mcg of sodium l-thyroxine intravenously and was begun on triiodothyronine 25mcg daily. Fluid intake was never restricted and was never below 1500cc daily. Sodium intake remained constant. Two days following the onset of thyroid therapy the urinary

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osmolality was equal to that of plasma and the serum sodium rose to 128mEq/liter prior to discharge. The urinary sodium on the day following thyroid therapy was 9mEq/liter. She was discharged on 120mgm of desiccated thyroid daily and approximately one month after hospital admission the serum sodium has risen to 138mEq/liter. Table 1 depicts the course of her serum sodium, osmolalities and intake and output.

Comments

Bartter and Schwartz[4] listed six cardinal findings in the syndrome of inappropriate secretion of antidiuretic hormone: (1) hyponatremia with corresponding hypo-osmolality of the serum and extracellular fluid, (2) continued renal excretion of sodium despite hyponatremia, (3) absence of clinical evidence of fluid overload, (4) osmolality of the urine greater than that appropriate for the concomitant plasma tonicity, (5) normal renal function, and (6) normal adrenal function.

Our patient entered the hospital with dehydration, an elevated blood urea nitrogen and a normal serum sodium. After hydration the sodium and the blood urea nitrogen dropped respectively to 129mEq/liter and 16mgm%. At no time was there edema or clinical evidence of overhydration despite the serum sodium falling to a low of 114mEq/liter. At this time the urine was definitely hypertonic to plasma. Primary hypothyroidism was documented by a low PBI and low radioiodine uptake without a significant response to thyroid stimulating hormone. The twenty-four hour urinary 17-hydroxy steroids were reduced. Low urinary steroids are a common finding in hypothyroidism[5], however the elevated serum cortisol and rise of serum sodium to normal without the administration of steroids helps rule out the diagnosis of adrenal insufficiency. The presence of FSH, failure to increase the thyroid uptake after thyroid stimulating hormone, and the normal size of the sella turcica are evidence against pituitary insufficiency. The low urinary sodium which was measured one day after thyroid therapy is the only disturbing feature of this case. Since no urinary sodiums were measured during the fall-off phase of the serum sodium one cannot predict how high the urine sodiums were during this time. However, patients with the syndrome of inappropriate secretion of antidiuretic hormone may reach a steady state when the serum sodium is low, sodium excretion diminishes, and a high urinary sodium is no longer found[6, 7]. Jaenike and Waterhouse[8] demonstrated that prolonged administration of pitressin ultimately caused a decline in urinary sodium and osmolality after the initial rise.

The usual and effective treatment for the syndrome of inappropriate antidiuretic hormone secretion is fluid restriction[9]. Usually hypertonic sodium replacement and/or administration of mineralocorticoids only raises the serum sodium transiently. In our case no fluid restriction was imposed. In fact, fluid intake was held at above 1500cc daily purposely. At no time did the patient receive hypertonic saline. Even though conventional techniques of treatment were not used, the serum sodium increased and urinary osmolality fell to below that of plasma with the use of thyroid therapy alone. The urinary osmolality dropped from 391 to 247 mosm/liter within 48 hours, and the serum sodium rose 7mEq/liter in the same time. All other factors remained constant. Over the preceding fifteen days the serum sodium had dropped 26mEq/liter prior to administration of thyroid.

The association of a low serum sodium with the inability to secrete a water load in myxedema has been recognized in the past[10]. Aikawa[11] described four of eight myxedematous patients with low serum sodium values ranging from 116 to 135mEq/liter. Two of those patients responded to thyroid therapy with elevation of the serum sodium. High values for radiosodium space appeared to correlate well with low serum sodium values. Holvey et al[12] reported a case of myxedema in whom the inappropriate secretion of antidiuretic hormone appeared corrected following l-thyroxine therapy. However, the patient also received prednisone and large

TABLE 1

SEQUENTIAL CHANGES IN URINE AND SERUM SODIUM AND OSMOLALITY BEFORE AND AFTER THYROID THERAPY.

Day	*Serum Sodium mEq/liter*	*Serum Osmolality mosm/liter*	*Urine Osmolality mosm/liter*	*Urine Sodium mEq/liter*	*Fluid Intake ml.*	*Urine Volume ml.*
1	140	—	—	—	—	—
4	129	—	—	—	—	—
7	125	—	—	—	—	—
10	123	—	—	—	—	—
15*	114	247	391	—	1500	1000
16	117	248	373	8.8	1600	800
18	120	248	247	15	1500	1250
22	125	—	—	—	—	—
26	128	—	—	—	—	—
30	138	—	—	—	—	—

* Sodium l-thyroxine 350mcg i.v.
Triiodothyronine 25mcg daily

amounts of sodium chloride in the course of therapy. Pettinger and colleagues (3) treated an elderly myxedemous female with all the criteria for this syndrome and noted a beneficial response to i.v. l-thyroxine. As in our case, water was not restricted but because of the severity of the patient's illness hypertonic sodium chloride was administered. Goldberg and Reivich[1] showed that alcohol administration to a myxedematous patient with hyponatremia lowered the urinary osmolality from 300 to 100mosm/liter in 45 minutes. Also, these authors found that triiodothyronine therapy would prevent hyponatremia despite liberal fluid intake. One study[13] presents evidence that the correction of the impaired water excretion in myxedema may take several months. However, the dramatic response in our patient and others[3, 12] to thyroid administration shows that this effect on antidiuretic hormone secretion may be rapid. It appears that the use of a fast acting parenteral thyroid preparation in hypothyroid patients with marked hyponatremia due to the inappropriate secretion of ADH may reverse this syndrome over a few days. The mechanism of inappropriate antidiuretic hormone in the face of low or absent thyroid hormone is yet to be elucidated.

Summary

A case of myxedema with marked hyponatremia is presented. Hyponatremia appeared to be secondary to the inappropriate secretion of antidiuretic hormone associated with myxedema. The administration of l-thyroxine intravenously plus oral thyroid therapy corrected this syndrome. This occurred even though fluid was not restricted and hypertonic intravenous sodium was not administered.

Acknowledgement

We are most grateful to Dr. Donald S. Dock for his encouragement and critical review of the manuscript, to Dr. John Milici for allowing us to study the patient, and to Mrs. Eleanor Cofrances for her expert secretarial assistance.

Generic and Trade Names of Drugs

Acetohexamide—Dyemelor
Sodium Levothyroxine—Synthroid
L-Triiodothyronine—Cytomel

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Methimazol Induced Aplastic Anemia

Arthur H. Rosenberg, M.D.

Synopsis-Abstract

A 21-year old female developed pancytopenia with a hypoplastic bone marrow during methimazol (Tapazol) therapy. She developed *Pseudomonas aeroginosa* pneumonia and septicemia. After a brief but near fatal illness, she made a rapid and complete recovery.

The following represents only the second reported case in the American literature of aplastic anemia associated with methimazol (Tapazole) therapy. The initial report by Levine and Rosenberg[1] appeared in 1954. In the German literature Klesse and Kruskemper[2] reported three cases of aplasia associated with methimazol.

Report of a Case

A 21-year old female was admitted to The Greenwich Hospital on October 9, 1967, with sore throat and fever of one weeks' duration. She had been seen by her physician on July 18, 1967, complaining of nervousness and a thirty pound weight loss. She was taking norethynodrel with mestranol (Enovid-E). A sinus tachycardia (130/min.) was noted. The serum protein-bound iodine was 9.2 μg/100 ml; white blood cell count (WBC) 5,800/cu mm; and the hemoglobin 14.4 gm/100 ml. A diagnosis of hyperthyrodism was made, and the patient was treated with methimazol, 15 mg three times a day, which she remained on until admission to The Greenwich Hospital. On October 2, 1967, she complained of a sore throat and was found to be febrile with a membranous pharyngeal exudate. She was given tetracycline (Tetracyn) 250 mg. orally four times a day for five days with no improvement. She was then treated with Penicillin 400,000 U., orally, four times a day until admission to the hospital.

Physical examination on admission to the hospital revealed an acutely ill female with a temperature of 102.8 F. (39.3 C). The gingiva were slightly hypertrophied. The tonsils were enlarged, red, with a yellow-white exudate. The tonsillar and anterior cervical lymph nodes were moderately enlarged and tender. The lungs were clear. The heart rate was regular at 120 beats per minute with a grade 2 mid systolic murmur along the left sternal border. The spleen tip was palpable below the left costal margin.

Laboratory studies revealed a hemoglobin of 8.5 gm/100 ml; hematocrit 26%; WBC 900/cu mm with 100% lymphocytes; platelets, 18,000/cu mm and reticulocytes 0%. Table I. The blood urea nitrogen (BUN), glucose, calcium and phosphate, uric acid, chest roentgenogram, electrocardiogram and spinal fluid were normal. A protein-bound iodine was 4 ug/100 ml. Serum protein electrophoresis revealed an albumin of 2.9 gm/100 ml, alpha 1 of 0.5 gm/100 ml, alpha 2 of 0.9 gm/100 ml, beta 0.8 gm/100 ml, and gamma globulin of 1.8 gm/100 ml. Sternal bone marrow aspiration showed a hypocellular marrow with clusters of small lymphocytes and mature plasma cells around scanty marrow spicules. Bone marrow biopsy from the posterior iliac spine showed marked hypocellularity with lymphocytes and plasma cells predominating; only a few myeloid cells and one megakaryocyte were seen. See Figure I. Throat culture revealed *Pseudomonas aeroginosa, coliform and B-hemolytic streptococci.* Stool, urine and blood cultures were negative.

The patient was felt to have aplastic anemia secondary to methimazol. Beginning on October 10th she received Tetracycline 250 mg, orally, four times a day. This was discontinued on October 12th and sodium colistimethate (Colymycin) 100 mg, intramuscularly, three times a day for six days was started. The following day (October 13th) sodium cephalothin (Keflin) 3 gm., intravenously, every six hours for 5 days was started. Nevertheless she had daily temperature spikes to 106 F with increasing weakness. Hydrocortisone, 50 mg. intravenously, every eight hours was given on October 14, 15 and 16, and fluoxymesterone (Halotestin), 10 mg orally three times a day was started on October 15th and continued through discharge. Six days following admission she developed physical and radiological signs of left upper and lower lobe pneumonia. She became hypotensive with readings between 80 and 100/50, associated with increasing lethargy, tachypnea and tachycardia. Penicillin, 600,000 U. intramuscularly, every six hours was immediately added to the antiboiotic regimen. On October 16th aqueous penicillin 10,000,000 U. per day was started intravenously and continued for five days. Seven days following admission she received the first of daily white cell concentrate transfusions in addition to periodic blood transfusions. (The white cell concentrates were prepared at The New York Blood Center by Dr. Carlo Ehrich. The daily concentrate transfusion was prepared by extracting the buffy coat from twelve healthy

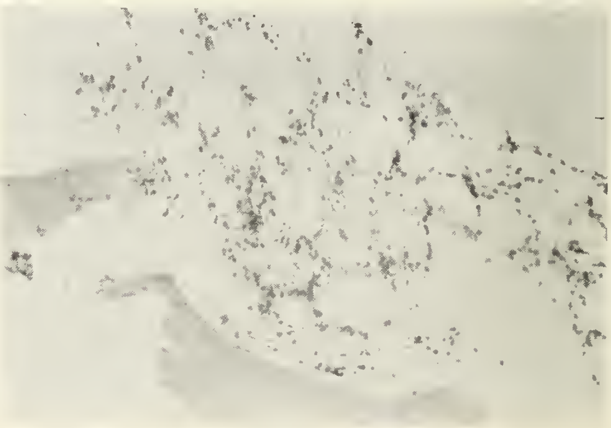

Figure 1
Bone marrow biopsy showing hypocellularity. (H&E 100 X).

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TABLE 1

HEMATOLOGIC DATA

Date	*Hemoglobin, gm/100 cc*	*Hematocrit, %*	*Reticulocytes, %*	*WBC, /cu mm*	*Segmented Neutrophiles, %*	*Band Neutrophils, %*	*Lymphocytes, %*	*Monocytes, %*	*Eosinophils, %*	*Platelets, /cu mm*	*Remarks*
10-9-67	8.5	26	0	900	0	0	100	0	0	18,000	2 units of packed red cells
10-13-67	10.0	30	0	900	4	0	92	4	—	8,000	1 unit of packed red cells
10-15-67	9.6	28	0	500	8	0	88	4	—	18,000	1 unit of packed red cells
10-16-67	10.5	32	0	800	6	12	82	—	—	18,000	1 white cell transfusion
10-17-67	10.7	32	0	1,200	22	11	64	—	3	—	1 white cell transfusion
10-18-67	10.4	33	0.1	1,600	42	24	34	—	—	42,000	1 white cell transfusion
10-19-67	10.8	33	0.3	2,000	30	50	19	1	—	25,000	1 white cell transfusion
10-20-67	10.0	32	0	2,000	36	20	40	2	2	37,000	1 white cell transfusion
10-21-67	11.6	36	0	3,100	26	30	44	—	—	28,000	
10-22-67	11.7	35	0.4	5,100	28	6	57	7	2	13,000	
10-25-67	11.0	34	0.5	5,800	44	2	46	8	—	16,000	
10-28-67	11.6	35	2.0	6,800	44	9	42	5	—	34,000	
11-22-67	11.8	37	0.6	4,500	37	—	63	—	—	170,000	
12-27-67	13.8	38	—	6,700	44	—	54	1	1	135,000	
4-8-68	13.0	39	—	5,100	72	—	28	—	—	135,000	

donors giving approximately a 65% recovery of white cells.) The blood count at this time showed a hemoglobin of 10.5 gm/100 ml; reticulocytes, 0%; WBC, 800/cu mm with 8% segmented neutrophiles and platelets, 18,000/cu mm. Despite the marked thrombocytopenia there was no gross bleeding. At this time sputum, blood and stool cultures were positive for *Pseudomonas aeroginosa*.

On October 18 the patient's condition seemed hopeless. The pneumonia had extended on the left side and was now present in the right lung. Cyanosis was present. However, the WBC was 1,600/cu mm with 42% segmented neutrophiles; 24% band neutrophiles and 34% lymphocytes. Sodium Colistimethate and Sodium Cephalothin were discontinued. Gentamicin (kindly supplied by Schering) 50 mg three times a day intramuscularly was started. On October 19 the patient appeared slightly improved and by October 21 she had made a startling recovery with normal temperature, respiratory rate and blood pressure, negative blood cultures and some resolution of the pneumonia. The WBC had risen to 3,100/cu mm with 26% segmented neutrophiles; 30% band neutrophiles; 44% lymphocytes. A sternal bone marrow aspiration revealed nests of erythropoietic and myeloid cells with a few young megakaryocytes, but cellularity was still reduced. The white cell transfusions, intravenous fluids and penicillin were discontinued. Gentamicin was maintained and the dose tapered gradually until October 26 when the drug was discontinued.

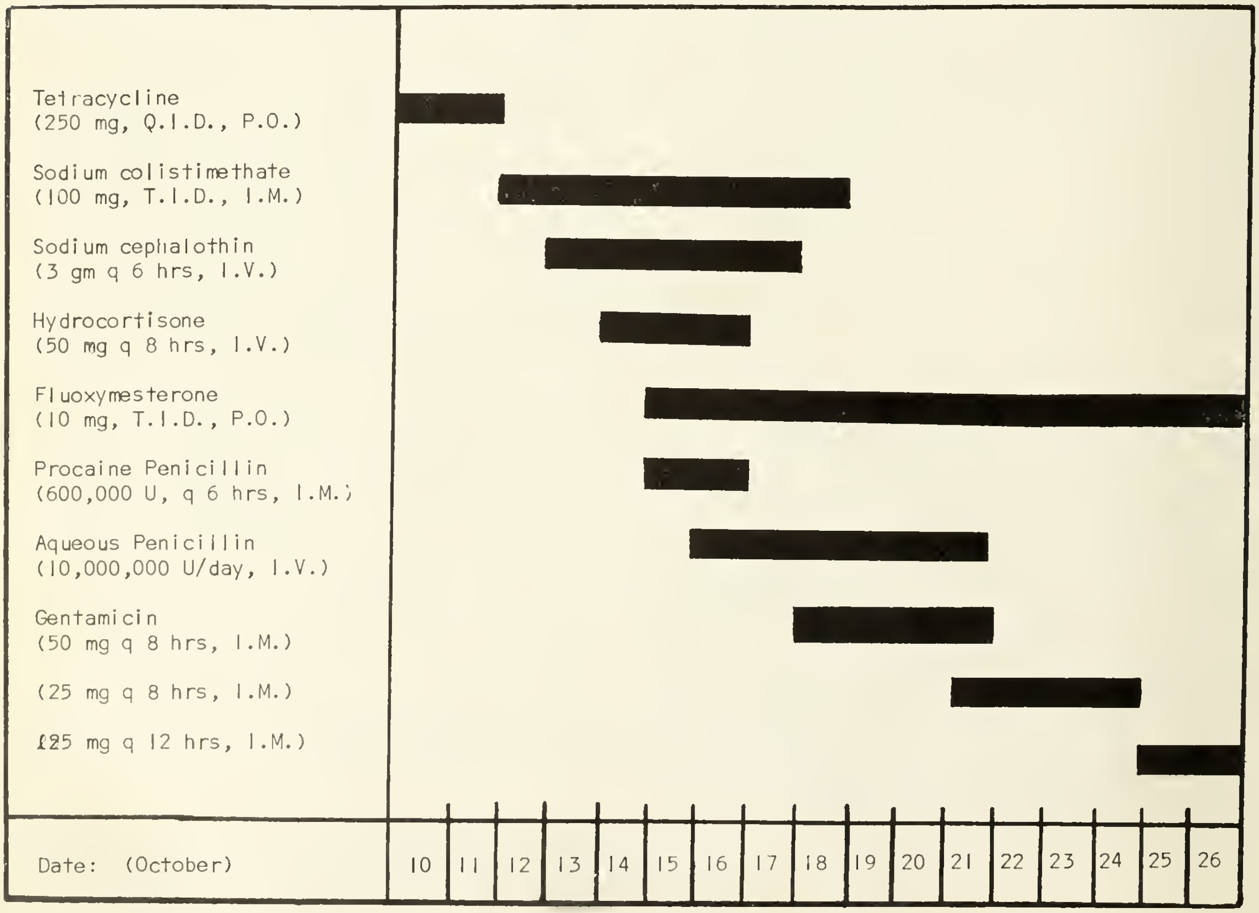
The patient was discharged on October 28, asymptomatic. She was maintained on fluoxymesterone 10 mg, three times a day. At discharge the hemoglobin was 11.6 gm/100 ml; hematocrit 35%; WBC, 6,800/cu mm with 44% segmented neutrophiles, 9% band neutrophiles, 42% lymphocytes, 5% monocytes, 2% reticulocytes and platelets, 34,000/cu mm. Since discharge the patient has remained asymptomatic. On April 8, 1968 the hemoglobin was 13 gm/100 ml; hematocrit 39%; WBC 5,100/cu mm with 72% segmented neutrophiles and 28% lymphocytes and platelets, 135,000/cu mm.

Comment

This patient was treated for hyperthyroidism with methimazol and subsequently developed severe pancytopenia with bone marrow hypoplasia, *Pseudomonas aeroginosa* pneumonia and septicemia. The initial diagnosis of hyperthyroidism is questionable since the patient was taking norethynodrel with mestranol at the time the protein-bound iodine was found to be slightly elevated. After nine months observation the patient has remained euthyroid without medication.

TABLE 2

DRUG THERAPY



It is difficult to say which of the therapeutic measures utilized were most instrumental to her recovery. The dramatic improvement following soon after changing from sodium colistimethate to Gentamicin may well have been based on drug superiority. Gentamicin is an experimental drug effective in pseudomonas infections.)[3] Nevertheless, increasing numbers of polymorphonuclear cells were appearing in the peripheral blood at that time, and that may have been the more important factor in the control of her infection. The benefit obtained from the white cell transfusions is also conjectural.

Martelo et al[4] reported the only case of aplastic anemia following propylthiouracil therapy, and in their case, the case of Levine and Rosenberg[1] and the present case, complete recovery rapidly occurred after discontinuing the offending drug. Levine and Rosenberg felt that cortisone was responsible for their patient's rapid recovery, but the patient reported by Martelo et al did not receive steroids and the present case received cortisone for only three days. This strongly suggests recovery was spontaneous and unrelated to cortisone therapy.

Unlike the cases reported in the American literature, all three cases noted by Klesse and Kruskemper[2] died. It is interesting to note the aplasia persisted until death in two cases (six weeks and 139 days); the third case report failed to state the time of death in relation to the onset of symptoms.

Agranulocytosis is a more frequent though still rare complication of antithyroid drug therapy, occuring in about one patient in five-hundred.[5] As in the cases of aplastic anemia, symptoms occur concurrently with drug therapy. Recovery is usually rapid and complete with only a rare death. Astwood[5] argues that since blood dyscrasias occurs so infrequently, and since cytopenia occurs so rapidly, routine blood counts are not indicated. Unfortunately in the present case and those of Levine and Rosenberg and Martelo et al, serial blood counts were not obtained prior to the onset of pancytopenia. Therefore, one is unable to know whether this precaution would have given the physician some warning of impending aplasia.

Generic and Trade Names of Drugs

Methimazol—Tapazole.
Norethynodrel with mestranol—Enovid.
Tetracycline—Tetracyn.
Sodium colistimethate—Colymycin.
Sodium cephalothin—Keflin.
Fluoxymesterone—Halotestin.

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"Ignorance is preferable to error; and he is less remote from the truth who believes nothing than he who believes what is wrong."—Thomas Jefferson. *Notes on the State of Virginia. Edited by W. Peden. Chapel Hill: University of North Carolina Press, 1955.*

Medical Grand Rounds
Yale-New Haven Hospital
A Case of Manic-Depressive Illness with Lithium Toxicity

Frederick Lee Sachs, M.D. and Lewis Landsberg, M.D., Editors
Pamela Brooten, Assistant Editor

The patient is a 54-year-old married woman who was admitted to the Yale-New Haven Hospital on June 19, 1969, in diabetic ketoacidosis. She had a long history of manic-depressive behavior, with her last manic episode occurring in the fall of 1968. She had been followed for her psychiatric disorder at The Connecticut Mental Health Center and was taking lithium carbonate 300 mg., five times daily. Blood levels of lithium on that dose were in the therapeutic range (between 0.54 and 0.72 milliequilavents per liter) .

Eight months before admission mild hypertension was noted and she was begun on Lasix 80 mg. by mouth daily. One month before admission glycosuria developed and she was placed on a 1200 calorie diet and Orinase 500 mg. by mouth twice daily. Blood sugars were never determined.

Three days before admission she developed increasing thirst and polyuria, became increasingly obtunded and was seen in the Emergency Room where Kussmaul respirations were noted. Her blood glucose was 972 mg.%, and the urine was 4+/large with a serum acetone of 1.16 and arterial pH of 7.08. Serum bicarbonate was 10 milliequivalents per liter.

On arrival on the Medical Service her diabetic acidosis responded to the usual treatment including 675 units of CZI insulin and 12 liters of fluid. She did well until 9 hours after admission, when she had two black, tarry stools accompanied by a fall in blood pressure from 130/90 to 90/60. Gastric aspirate revealed one liter of bright red blood. Gastroscopy, esophagoscopy, and upper GI series all failed to reveal the site of bleeding. She received 4 units of blood with a return of her vital signs to normal. Bleeding did not recur.

On the second hospital day the patient was restarted on 1500 mg. of lithium daily and a lithium level on Day 5 was 0.82 milliequivalents per liter, well within the therapeutic range. On the eighth hospital day the patient was noted to have an output of 6 liters despite the absence of glycosuria. Skull x-rays were normal. Serum cortisols were normal but did not show the expected diurnal variation. A water deprivation test demonstrated a 7¼ pound weight loss over 12 hours with failure to concentrate the urine, the highest osmolarity recorded being 208 milliosmoles at 9 hours. BUN before water deprivation was 7 mg.% and rose to 15 mg.% following deprivation. There was a corresponding rise in serum sodium from 136 milliequivalents per liter to 150 milliequivalents per liter. Serum osmolarity rose from 296 to 324 milliosmoles. Failure to concentrate the urine was also demonstrated following the administration of Pitressin tannate in oil and aqueous Pitressin. Thyroid function studies included a PBI of 5.2 micrograms % with a T3 100%. RAI uptake showed 8% uptake at 2 hours, 9% at 6 hours, and 16% at 24 hours, a borderline low-normal study.

She convalesced well until the 29th hospital day when she was noted to be markedly obtunded with hypereflexia, tremulousness, myoclonic jerks, and unsustained ankle clonus. Serum litium level at that time was markedly elevated at 3.04 milliequivalents per liter. A lumbar puncture was unremarkable except for a protein of 89 mg.%. The cerebral spinal fluid lithium level was 1.24 milliequivalents per liter. ECG revealed nonspecific T wave flattening and EEG showed marked diffuse slow and sharp waves, consistent with lithium toxicity. Lithium was discontinued and the patient was begun on a saline diuresis. She demonstrated gradual improvement and by the 33rd hospital day the lithium level was 0.49 milliequivalents per liter and she had returned to her base line status.

Several days after the return to normal lithium levels she was begun on Haloperidol because of the development of hypomanic behavior.

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DR. LEWIS LANDSBERG, Chief Resident, Department of Medicine, Yale University School of Medicine, New Haven, Connecticut.

DR. LEWIS LANDSBERG: Dr. Patrick McKegney will open the discussion.

DR. PATRICK McKEGNEY: It is apparent that we lost track of the lithium. We assumed, because she had been taking the same dose of lithium for over a year with normal lithium levels, that she would maintain this normal level indefinitely. We did not obtain weekly lithium levels beyond the first two determinations and don't know when her lithium level began to rise. Several factors might be implicated; she had undergone a water deprivation test, had severe diarrhea and developed a large diuresis. Intakes and outputs were only estimates, since she was quite uncooperative. Her intoxication with lithium responded characteristically to cessation of the drug and administration of parenteral fluids. Lithium levels were normal within five days and she began to show signs of hypomanic behavior at the end of this period.

The most recent and comprehensive review of lithium toxicity is a summary of eight cases from Denmark collected over a ten year period.[1] These cases demonstrate a wide range of signs and symptoms. The prodromal symptoms include sluggishness, drowsiness, a coarse tremor, myoclonic muscle twitching, dysarthria, loss of appetite and diarrhea. Although not seen in the above series, other authors have also mentioned polyuria and polydypsia as prominent in the prodromal period. In the full-blown syndrome, obtundation leads to a characteristic type of coma: the patient can be roused with effort and will respond as long as vigorously stimulated. Once the stimulus disappears, the patient lapses into coma once more. This is the type of coma one sees with phenothiazine or tricyclic antidepressant toxicity. Coarse tremor of a clonic type, EEG demonstrating slow wave activity, transient renal insufficiency, and gray-ashen appearance characterize this condition. Not all of these signs and symptoms are seen in every case of lithium toxicity. The patient today demonstrated more signs than any patient described in the literature. Although the level of lithium can be lowered rapidly with forced diuresis, this itself may not be sufficient to save the patient since one patient in the Danish series died in spite of this procedure. The syndrome of lithium toxicity develops over several days and requires several days to disappear. Despite vigorous treatment, intoxicated patients are obtunded over a significant period of time and are prone to develop pneumonias and urinary tract infections.

A PHYSICIAN: Under what circumstances might lithium be used clinically?

DR. McKEGNEY: The only indication for lithium carbonate is manic-depressive illness.

DR. LANDSBERG: Dr. Demers will present data on the physiology and biochemistry of lithium.

DR. DEMERS: Lithium is a small metallic element with an atomic weight of 7. It is primarily excreted by the kidneys and skin. The amount of salt in the diet profoundly affects the excretory rate of lithium and lithium accumulation has been reported in patients on low-sodium diets. Studies at The Connecticut Mental Health Center have shown that placing a patient on 92 to 96 milliequivalents of sodium a day will raise the lithium level about 20%. Raising the sodium intake to above 200 milliequivalents of sodium per day will reduce the lithium values considerably with corresponding increase in lithium clearance.

Carbohydrate metabolism is also altered. There is a decreased sensitivity to insulin as evidenced by an abnormal insulin tolerance test in patients on lithium. Patients on chronic lithium therapy have a decreased rate of glucose utilization as determined by the I.V. glucose tolerance test. Even more significantly, increased levels of insulin were detected during the I.V. glucose tolerance test. This suggests interference between lithium and insulin utilization.

Central nervous system effects[2] are demonstrated in animal subjects taking lithium. Lithium has been shown to produce a shift in norepinephrine metabolism from O-methylation to intraneural deamination in the rat brain, which suggests that lithium may decrease available norepinephrine at central synaptic receptors. Lithium depletes norepinephrine at nerve terminals. Katz and co-workers[3] have shown that lithium in low concentrations inhibits the electrically-stimulated release of norephrine and serotonin in rat brain slices. It would appear that lithium affects the availability of norepinephrine at central nervous system receptor sites.

The catecholamine hypothesis of affective disorders postulates that in depression there is a deficiency of free, available norepinephrine at central synaptic receptors. During manic episodes, there may be execessive available catecholamines at the central synapse. If this hypothesis is true, then lithium prevents recurrent manic episodes by reducing availability of norepinephrine at central nervous system receptor sites.[4]

A PHYSICIAN: How can one explain the polydypsia and polyuria seen in this patient?

DR. DEMERS: Probably by lithium antagonism to Pitressin. When rats are intoxicated with lithium they develop polydypsia and polyuria which is Pitressin-resistant. The simultaneous administration of intravenous lithium and Pitressin eliminates the effects of Pitressin as evidenced by failure to increase urine osmolarity or decrease urine volume.

DR. LANDSBERG: Dr. Thomas Detre will continue the discussion.

DR. THOMAS DETRE: As Dr. McKegney has mentioned, lithium carbonate is the treatment of choice in manic-depressive illness. It is not yet marketed in the United States for a number of reasons. In the first place, it arrived on the scene with a somewhat tarnished reputation, having been unsuccessfully tried previously in seizure disorders and having caused fatalities when used as a salt substitute in cardiac and renal patients. Furthermore, it is a very inexpensive element and until recently the major drug companies have been hesitant to invest the necessary funds required for the marketing of this drug.

The classical indication for lithium carbonate is manic-depressive illness. The significance of finding a reasonably effective drug cannot be sufficiently emphasized since this is a disease which runs a rather violent course throughout young adult life. The syndrome consists of episodes during which the patient has varying degrees of mood disturbances, being either depressed or "high". Only rarely does the illness manifest itself in only one type of mood disorder. Each episode may last from several weeks to several months and their duration tends to increase with age. There is usually a symptom-free interval between the attacks or at least following each manic and depressive attack (if the patient first has one and then another type of attack). In more malignant cases, however, one type of mood disturbance rapidly follows the other and there is practically no time when the patient feels normal.

The acute phase of manic-depressive disease is treated by administering lithium in doses of 1200 and 1800 mg. with the idea of achieving a serum level of 1.5 mEq/1. At this dose level the patient becomes mildly toxic. He may, for instance, feel somewhat sluggish, have mild nausea and some tremor. Sometimes, when levels of 2 or even 2.5 mEq/1 must be reached to break the manic cycle, more severe toxic symptoms already described by Dr. McKegney may appear. Since it takes 5 to 10 days to achieve a therapeutic effect, regardless of what dose is used we prefer to give lithium carbonate in doses sufficient to achieve 1.5 mEq/1 concomitantly with a major tranquilizer (such as Haloperidol or a phenothiazine) or ECT if the patient's behavior is disruptive, to avoid the uncomfortable and potentially hazardous toxic symptoms. Once the acute episode is over the dose is lowered to achieve a serum level of —.8 —1.2 mEq/. On this maintenance dose mood swings can be completely prevented in about 65% of the cases and in another 15% symptoms become sufficiently mild to avoid hospitalization.

Lithium has been used experimentally in other psychiatric disorders. The drug has been found effective in cyclothymic personality disorders and in a number of other conditions with a periodic course in which episodes characterized by insomnia, and psychomoter overactivity alternate with hypersomnia and apathy .

A PHYSICIAN: Does lithium have a role in depression?

DR. DETRE: Yes, there are at least two subtypes of depression. One is recurrent endogenous depression characterized by psychomotor agitation ,insomnia and anorexia. In these cases lithium appears ineffective. Another type of recurrent depression characterized by hypersomnia, apathy, and in some cases overeating, the characteristics usually found in patients who have both manic and depressive episodes, responds well to lithium but not as well as the manic phase of the disease.

A PHYSICIAN: When we referred to the doses of lithium, are we speaking of lithium per se or lithium carbonate?

DR. DETRE: Lithium carbonate.

A PHYSICIAN: In a manic-depressive, is the drug equally effective if you start in the depressive phase versus starting in the manic phase?

DR. DETRE: It is equally effective in preventing further recurrences of manic episodes, regardless in which phase of the disease treatment is initiated.

A PHYSICIAN: What is its effect on the depressive phase?

DR. DETRE: Decreases depressive mood, anergia, and hypersomnia, without producing euphoria.

A PHYSICIAN: It was stated that this patient became high just three days after lithium was discontinued. I believe that lithium has been shown to be stored in tissue during periods of acute mania. Why did she become manic so rapidly?

DR. McKEGNEY: I do not wish to leave the impression that this woman was classicly manic after three days off lithium. It was her family who informed the attending physician that she was exhibiting certain behavior suggestive of an early manic state. We would have missed this finding.

A recent publication[5] documents the occurrence of an exacerbation of the manic state 12 hours after the discontinuation of lithium at a point when the lithium level was undoubtedly falling but still theoretically in a therapeutic range.

DR. CHASE KIMBALL: The possibility exists that the patient's family confused an acute organic brain syndrome with previous manic behavior.

A second point is that hyperglycemia has been detected in patients with manic-depressive illness. This finding has been attributed to impairment of glucose utilization and variation in serum insulin levels.

What was the status of her renal functions just before her hospital admission?

DR. HOWARD LEVITIN: We believe that her renal function prior to admission was good. This is best illustrated by the fact that she was able to dilute her urine to around 60 or 70 milliosmoles during a period of excessive fluid intake. Maximal dilution is as good an index of renal function as the water deprivation test. She was taking 1,500 milligrams of lithium daily and excreting it quite well until she got dehydrated in association with her diabetic acidosis. Continued administration of the same dose of lithium at a time when she was unable to excrete the drug properly produced the toxicity. Any time there is a change in renal function we must ask two questions: 1) What drug is the patient taking that might have caused the change in function; and 2) Is the patient taking a drug whose excretion will be altered by the drop in renal filtration?

DR. PHILIP K. BONDY: What we are saying about lithium today closely resembles what was said about bromides in years past. The toxicities of these two compounds are really quite similar.

I am very skeptical that the lithium triggered this episode of diabetic acidosis. The patient had been maintained on the same level of lithium for a long period of time and yet when she entered dehydrated and in acidosis her lithium level was not remarkably elevated. It seems highly unlikely that lithium produced a chemical abnormality of this degree.

DR. SAMUEL KUSHLAN: I think it is important to mention that hemorrhagic gastritis has been reported in patients with diabetic acidosis and may have accounted for her episode of upper GI bleeding.

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Anesthesiology Grand Rounds
Yale-New Haven Hospital

Hypothermia for Excision of Hepatic Artery Aneurysm

Samuel M. Lerner, M.D., Allen L. Toole, M.D., and Frederick W. Hehre, M. D.

Case Presentation

A 47 year old obese male was admitted to the Yale-New Haven Hospital with a known aneurysm of the hepatic artery. Two months previously the patient underwent an uneventful cholecystectomy, when the aneurysm was discovered. Since repair of the aneurysm would necessitate occlusion of blood flow to the liver, and require the use of hypothermia, it had been decided to discharge the patient and readmit him for aneurysmectomy at a later date.

Past history revealed only an appendectomy in 1943 and a laminectomy for herniated nucleus pulposis in 1957. Physical examination and laboratory data were considered to be within normal limits. Celiac arteriography revealed a fusiform aneurysm in the region of the right hepatic artery. (Fig. 1). Since the patient had received halothane two months prior, nitrous oxide was chosen as the primary anesthetic agent.

The patient was premedicated with pentobarbital,, 150 mg; morphine, 10 mg; and scopolamine, 0.5 mg intramuscularly. Anesthesia was induced with thiopental, 250 mg, I.V., and maintained with nitrous oxide and oxygen at 5 liter: 2 liter flow rate. Succinylcholine 50 mg. was used to facilitate endotracheal intubation. Chlorpromazine 20 mg was administered to facilitate cooling. Mannitol 10 gm was given for its renal protective effect. A total of 45 mg of curare was given to prevent shivering and to provide muscular relaxation during the operation.

The patient was cooled with a hypothermia blanket to an esophageal temperature of 30.5°C over a period of 5 hours and 5 minutes and maintained at that temperature for one hour and ten minutes. After heparinization, an end-to-end anastomosis was performed after excision of the aneurysm. The hepatic arterial circulation was completely interrupted for 24 minutes, and then intermittently for 50 minutes while hemostasis was secured.

At the end of the eight hour anesthetic, with the patient's temperature 34°C, 1 mg of atropine and 2.5 mg of prostigmine were given to reverse the curarization and the patient was extubated. He was admitted to the recovery room awake and talking. Pathologic examination showed the aneurysm to be arteriosclerotic.

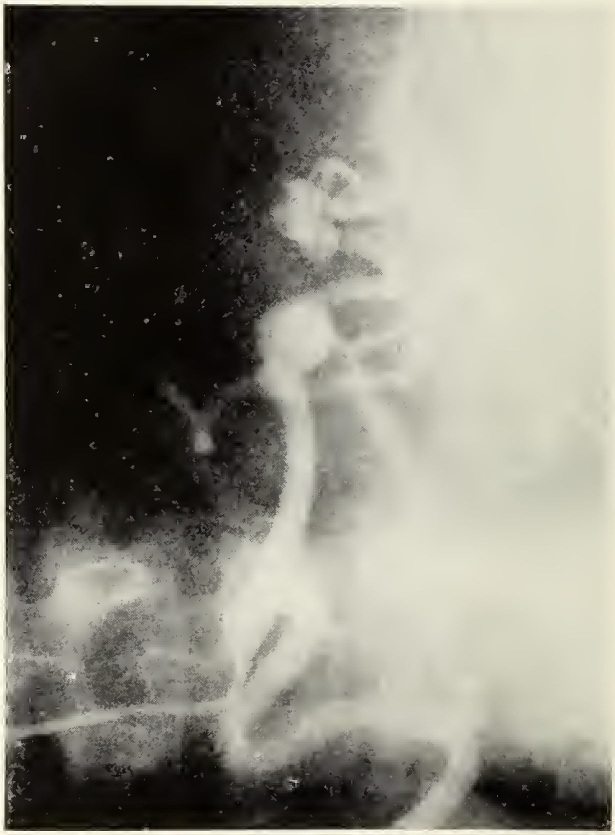

Figure 1
Preoperative coeliac artery arteriogram showing the aneurysm of the hepatic artery.

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Post-operatively he developed thrombophlebitis in his left leg. Following a femoral retrograde arteriogram he developed arterial thrombosis that required an open thrombectomy. He was discharged on the 20th post operative day.

Dr. Samuel M. Lerner:

The effect of temperature on chemical reaction rates is commonly expressed by the temperature coefficient, or Q10, which is the ratio of reaction rates at two temperatures separated by 10°C. The Van't Hoff rule states that the Q10 for chemical reactions is 2, and, therefore, the reaction rate is doubled for each 10°C rise in temperature or halved for each 10°C decline in temperature. Michenfelder and Theye have shown that the Q10 for metabolic reaction rates is also 2.[1] In other words, metabolic reaction rates and tissue oxygen consumption decrease exponentially with decreasing temperature. The reduction in metabolism is paralleled by a depression of the activity of cells and organs.

Pulmonary Function: Comroe[2] suggests that the progressive decrease in tidal volume and frequency of ventilation that occurs during hypothermia may be due to selective blockade of the medullary chemoreceptor response to arterial pCO_2. Anatomic deadspace is increased 50% as a result of bronchodilation.[3]

Circulation: There is a progressive bradycardia with decreasing temperature and serious arrhythmias appear below 30°C. The decreased cardiac output parallels the decline in heart rate, leaving stroke volume relatively unchanged.[4] The viscosity of the blood increases as temperature falls resulting in increased peripheral resistance. Consequently, there is only a moderate fall in arterial blood pressure despite the larger reduction in cardiac output.[4]

Renal Function: Renal plasma flow decreases, corresponding to the reduction in cardiac output with falling temperatures. This results in reduction of glomerular filtration and decreased urine production. Hypothermia exerts a direct depressant effect on tubular transport mechanisms reducing the reabsorption of sodium and water. As a result, the volume of urine produced is unaffected by hypothermia.[4]

Nervous System: Hypothermia depresses neuromuscular transmission and slows conduction of peripheral nerves. Cerebral activity, blood flow, and oxygen consumption decrease with lowered temperatures.[5]

Hepatic Function: The metabolic activity of the liver is reduced as measured by bile secretion, BSP clearance, and drug detoxification.[4] The total blood flow to the liver is normally 1500 ml per minute, of which 20% is supplied by the hepatic artery and 80% by the portal vein delivering blood that is 85% saturated with oxygen.[6] Of the 60 ml of oxygen consumed by the liver per minute, 43 ml are furnished by the portal vein.[6] In our patient, only the hepatic artery was occluded, and the continued portal vein blood flow allowed a longer period of arterial occlusion. Under experimental conditions, occlusion of blood flow to the liver for periods up to 60 minutes at 30°C has been shown to be safe.[7]

Thermoregulation: Lowering the environmental temperature causes stimulation of cold sensitive receptors in the skin and cooling of blood in the skin vessels. Thermoregulatory centers in the hypothalamus respond to afferent nervous impulses from the skin, and to the lower temperature of blood arriving from the periphery. In order to preserve core temperature, the hypothalamus acts to decrease heat loss by cutaneous vasoconstriction, and to increase heat production by shivering and increased metabolism. These mechanisms are quite effective. For example, heat loss from the hands and feet may be reduced by vasoconstriction to 2% of the total heat loss; although hand and foot surface area is 15% of the total body surface area. Shivering can cause a 500% increase in metabolic heat production.[8] Vasoconstriction is mediated by the sympathetic nervous system which can be blocked by chlorpromazine. The mechanism of shivering is not clear, but the final pathway is the lower motor neuron which can be blocked by curare.

Choice of Anesthetic Agents: Halothane is generally considered the anesthetic agent of choice for hypothermia. The actions of halothane include depression of the thermoregulatory centers,[6] peripheral vasodilatation,[9] and its anesthetic potency permits the administration of high concentration of oxygen. But since halothane has been associated with hepatic necrosis after repeated administration, it was decided to use a non-halogenated anesthetic agent in this patient.[10] Nitrous oxide was chosen as the principal anesthetic, supplemented with chlorpromazine and curare. Since anesthetic requirements are reduced during hypothermia, nitrous oxide in a 50% concentration is an effective agent.[11,12]

Slater, et al. have shown that hypoxia can be prevented in abdominal surgical cases where nitrous oxide was the principle anesthetic when not less than 33% of oxygen is used in the inspired anesthetic mixture.[13] Hedley-Whyte et al. reported that hypothermia has no significant effect on pulmonary shunting as long as controlled ventilation with appropriate tidal volumes are employed.[14]

Fractional doses of chlorpromazine were used during the induction of hypothermia to depress the thermoregulatory centers of the hypothalamus and to cause vasodilatation.[15]

Thiopental was considered safe for induction since recovery from its effect is dependent more on redistribution than metabolism in the liver. Curare was administered to prevent shivering during induction and to provide relaxation during operation.

Hypothermia brings about two basic changes in oxygen transport: (1) solubility of oxygen increases with decreasing temperature, and (2) there is a shift to the left of the oxyhemoglobin dissociation curve. For any given level of pO_2 in the tissues, the unloading of oxygen will be reduced. Consequently, a low level of oxygenation would be expected during hypothermia. This is countered by the increased amount of dissolved oxygen and by any increase in anaerobic metabolism which would lower the pH and shift the oxyhemoglobin dissociation curve back to the right.

The oxyhemoglobin dissociation curve is not fixed; it changes with pH, pCO_2, and temperature. The effect of pCO_2 on the curve has led some investigators to recommend that CO_2 be added to the inspired mixture in order to facilitate the unloading of oxygen during hypothermia.[11] According to Brewin the increased amount of CO_2 carried in solution at lower temperatures does not give rise to a respiratory acidosis because of the increased activity of hemoglobin buffers at reduced temperatures.[4]

In summary, a case was presented where hypothermia was employed to facilitate repair of an hepatic artery aneurysm. Nitrous oxide was shown to be a safe and effective anesthetic agent with little danger of hypoxia.

Discussion

Dr. Frank Manthey: Did you use the Blockaid monitor on this patient?

Dr. Lerner: The Blockaid monitor was used during the entire procedure. Curare is less effective at reduced temperature and we wanted an objective measurement of muscular relaxation.

Dr. Nicholas Greene: Suppose curare had not been administered. What happens to the response to nerve stimulation with decreasing temperature in the absence of curare? The response is probably different when the temperature decreases. Under these conditions, the Blockaid monitor would be of negative value. If there was not a normal motor response to nerve stimulation, somatic muscle function would be impaired and you would probably have surgical relaxation. But one could not say whether the abnormal response to nerve stimulation was due to hypothermia or to curare.

Dr. Alan Goldberg: One has to consider something that is as not widely appreciated, which Katz has shown. A normal individual, who has not received any muscle relaxants, can exhibit fade with tetanic stimulation and post-tetanic facilitation so that controlled observations have to be made before you administer any relaxant.

Dr. Manthey: You gave Thorazine and then paralysed him with curare. Wouldn't the curare have effectively blocked all this shivering without the Thorazine?

Dr. Lerner: Chlorpromazine serves two functions: It depresses the thermoregulatory center in the hypothalamus and provides vasodilatation which facilitates the transfer of heat from the body core. Curare was administered during the induction of hypothermia to prevent shivering, and continued during operation to provide muscular relaxation.

Dr. Michael Brecher: Aren't short acting barbiturates dependent upon liver for metabolism? Would you use smaller doses or would the re-distribution factor keep you out of problems?

Dr. Greene: I would anticipate that the magnitude of response to barbiturates or to any drug metabolized by the liver will not be affected by hypothermia. But the duration of response will be affected. The magnitude of response to morphine, Pentothal. or other non-soluble intravenous compounds will not be affected by hypothermia as much as duration of action.

Dr. Brecher: What was the dose of pentothal?

Dr. Lerner: The induction dose was 250 milligrams.

Dr. Koretada Kondo: I think the dose you used would not present much problem because you are not going to cool the patient before induction, and, if takes time to cool down the patient after induction.

Dr. Goldberg: What was the lowest temperature?

Dr. Lerner: 30.5°C.

Dr. Kondo: I missed the monitoring system. Did you have arterial line?

Dr. Lerner: I didn't discuss the monitoring system.

Dr. Greene: Would you? What should we monitor when we make a patient hypothermic?

Dr. Lerner: We routinely monitor the blood pressure, electrocardiogram and temperature.

Dr. Greene: Where was the temperature measured?

Dr. Lerner: Esophageal temperature.

Dr. Greene: Where was the blood pressure monitored?

Dr. Lerner: At the brachial artery, by sphygomomanometry.

Dr. Kondo: Direct measurement of arterial blood pressure is rather essential when the patient is hypothermic, since indirect measurement is not accurate because of constriction of peripheral arteries. Can you get a continuously accurate reading with a cuff? A systolic pressure of 90 mmHg with a cuff may not be this low on direct measurement.

Dr. Greene: I would opt for direct arterial pressure recordings during induced hypothermia. Even in the absence of blood loss, I would want an accurate measure of blood pressure.

There is controversy regarding management of pulmonary ventilation during hypothermia. One of the principle dangers of hypothermia is production of ventricular arrhythmias, including fibrillation. This is, in part, a function of temperature: the lower the temperature, the more frequently hypothermia is associated with arrhythmias. Arrhythmias are not common above 30°C. The temperature gradient across the myocardium may influence the onset of arrhythmias, also this is a function of the rate at which hypothermia is induced. If the temperature falls rapidly, the temperature gradient between the endocardium and epicardium will be greater than if the temperature is reduced slowly, and the likelihood of arrhythmias is greater. Also to be considered is the effect of carbon dioxide tension on development of arrhythmias during hypothermia. This is a function of how ventilation is managed. It has been said that if the patient is not hyperventilated during hypothermia, ventricular arrhythmias are more frequent, but the exact opposite has also been claimed: unless pCO_2 is normal or even slightly elevated during hypothermia, arrhythmias will occur. This controversy is compounded by the complexities inherent in arterial pCO_2 measurement during hypothermia. What is the value of monitoring arterial pCO_2 during induced hypothermia?

Dr. James Drews: What does pCO_2 mean at this temperature? Carbon dioxide production is going to be less so you have to keep pCO_2 in the same range. Should it build up a little more?

Dr. Greene: I give you a syringe containing blood that was removed from a patient at a temperature of 27°. What do you do with it?

Dr. Drews: I warm it to body temperature.

Dr. Greene: Yes, warm it to 37°C and then measure the pCO_2 in the blood at 37°C. What does this tell us about the pCO_2 in the patient at 27°C? This is what we care about.

Dr. Drews: When it is warmed do they allow some of the CO_2 to escape?

Dr. Greene: No. If one measures pCO_2 at 27°C, it is difficult to interpret the significance of the pCO_2 value obtained. The effect of change in temperature on the solubility of pCO_2 and on the dissociation of carbonic acid is complex. An exquisitely complicated nomogram has been developed in an attempt to relate changes in temperature to changes in pCO_2 and pH. But despite this monitoring pCO_2 doesn't really accomplish a great deal during induced hypothermia, because you don't know really in what context to put the results.

Dr. James Gilman: Gollin, in Florida, feels so strongly about this that he adds CO_2 to the inhaled mixture, because he feels that you should maintain a "normal" tension which means that there will be a vastly increased CO_2 content. Cool somebody down by 10°C and the solubility rises so much that CO_2 content has to rise tremendously to get a tension that is almost normal. He feels this is necessary, and he tries to maintain "normal" pH. Again you make use of the same correction factors. Electrode characteristics, and the membrane characteristics, all change when temperature changes. Since there is decreased CO_2 production, and increased solubility of CO_2, low pCO_2 is not a problem. Trouble begins when these patients are warmed. Then CO_2 returns to the blood stream that has been sequestered in areas where the peripheral perfusion has been poor and there may be rapid drops in pH, causing arrhythmias and hypotension.

Dr. Drews: There is more dissolved CO_2 at lower temperatures with a low CO_2 tension. Now warm this up in a closed system. Wouldn't this reading come out as a high pCO_2?

Dr. Gilman: Correct. Warm this blood and the pCO_2 goes up. The content in the syringe never changes, because it is a sealed system. The *tension* is different and the correction factors take this into account.

Dr. Greene: During induced hypothermia, not only does the solubility of CO_2 and oxygen in blood change, but also the solubility of all anesthetic agents changes. This is one of two reasons why a patient who is hypothermic needs less anesthetic. The lower the temperature becomes, the greater the solubility, so that at any given concentration of anesthetic in the inspired air, there is more anesthetic in the blood as the blood becomes cooler.

Dr. Drews: Isn't it the tension of the anesthetic agent that gives you your anesthesia? Although you take more and more in, there is less tension, you need more anesthetic.

Dr. Greene: If one takes olive oil and exposes it at a fixed temperature, one can measure a solubility of, say, halothane in olive oil. When one lowers the temperature of olive oil, the same content will be associated with lower tension, but if you expose it to the same tension there will be a greater content. So at the cellular level, as temperature goes down, tension should go up, too, because content and tension are always going to be equated. But, a patient needs less anesthetic as he becomes hypothermic for two reasons. One is that hypothermia per se is producing an analgesic or anesthetic effect, and secondly, the hypothermia alters solubility of the anesthetic. The way this patient was anesthetized, with nitrous oxide and curare, is safer than using an anesthetic such as halothane was used, in my opinion, because the effects of hypothermia on the solubility of a potent anestheic such as halothane are such that one has to decrease halothane concentration as the temperature goes down to compensate for the increase in solubility. If one continues to give halothane for a long period of time to a patient who is hypothermic, the amount of halothane taken up that patient, will be considerable. From a clinical point of view there is also a great deal to be said for using curare as a muscle relaxant during hypothermia rather than succinylcholine because the factors affecting duration of action of curare are not as temperature dependent as the factors affecting the duration of action of succinylcholine. Succinylcholine is inactivated by enzymes which are affected by temperature and I would suggest use of relaxants eliminated by non-enzymic means.

Dr. Kondo: What about intravenous anesthetics or neuroleptoanalgesics, like Innovar, when you are using hypothermic technique? It is easy to overdose with the inhalation anesthetics because hypothermia alters solubility of inhalation anesthetic and cardiac output. How about using a set dose of intravenous drugs, like Innovar and curare.

Dr. Greene: Set dose? According to what standard?

Dr. Kondo: Doses on a milligram per kilogram basis.

Dr. Greene: If set or determined in a normothermic patient, I would feel uncomfortable using the same dosage schedule in a hypothermic patient because duration of action of a compound such as Innovar is related to its rate of enzymic destruction, a rate which is temperature dependent. Innovar might prove useful as a basal anesthetic while inducing anesthesia or during cooling, but its repeated administration after establishment of hypothermia might prove dangerous.

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X-Ray of the Month

Section of Chest Diseases

Arnold B. Rilance, M.D.

History

G.M., #75-05-39. A 16 year old male was admitted to the Yale-New Haven Hospital with a history of blurred vision of 1 to 2 months duration. In addition he had noted congestion of the conjunctiva and a productive cough. There was some dyspnea on heavy exertion. There was no history of parotid enlargement, skin rash, arthralgia, subcutaneous nodules, lymphadenopathy, chills or night sweats.

When seen in the Opthalmology Clinic on 5/16/69, an acute uveitis had been demonstrated with "mutton fat" opacities in the cornea.

His blood serology and skin tests for tuberculosis, brucillosis, coccidiomycosis, histoplasmosis and blastomycosis were all negative. A chest X-ray showed changes compatible with sarcoidosis.

Physical Examination:

Demonstrated a few shotty posterior cervical, axilliary and inguinal lymph nodes. The chest was normal in all respects. The liver and spleen were not palpable.

Laboratory Tests:

Including CBC, urinalysis, BUN, FBS, electrolytes, serum calcium and liver function tests were normal. Serum electrophoresis was normal.

Liver Biopsy:

Large granulomata containing giant cells, epithelioid cells and lymphocytes, non-caseating in type, felt to be consistent with sarcoidosis.

Conjunctival Biopsy:

Chronic inflammation—not diagnostic of sarcoid.

Pulmonary Function Tests:

Revealed a severe restrictive defect with only minimal airway obstruction and only a minimal reduction in maximum voluntary ventilation.

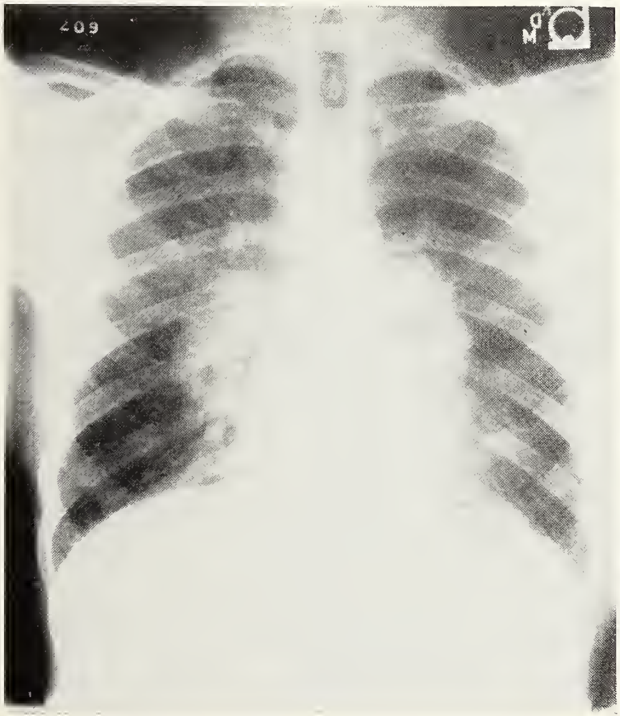

Figure 1

Demonstrates the typical pattern of pulmonary sarcoid with a fine miliary infiltration in both lungs, large "potato" nodes in both hila and moderate broadening of superior mediastinal shadow.

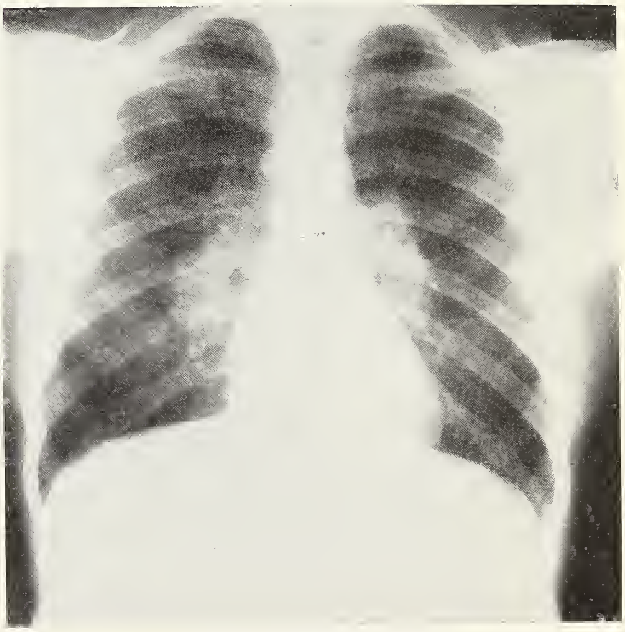

Figure 2

Appearance of P.A. projection after 3 months treatment with prednisone. Marked regression of pulmonary infiltrates and size of hilar and mediastinal nodes.

DR. ARNOLD B. RILANCE, Director. Winchester Chest Clinics, Yale-New Haven Medical Center.

Arterial PO_2—90; PCO_2—36 Arterial PH—7.44

Pulmonary diffusion capacity—21 (normal—17)

The patient was started on Prednisone, 40 mg. per day, with INH, and discharged to be followed in the Winchester Chest Clinics.

Diagnosis

Sarcoidosis—involving lungs, hilar and mediastinal nodes, with bilateral granulomatous uveitis. An unusual problem in this adolescent age group.

Discussion

Sarcoidosis is relatively rare in children. It is predominantly a disease of the Negro race and most prevalent in the South Atlantic and Gulf states, though it occurs sporadically elsewhere.

Sarcoidosis is a systemic disease or group of diseases of undetermined etiology. Histologically, it is characterized by the presence of epithelioid cell tubercles and giant cells showing little or no necrosis. Clinically, the disease may involve lymph nodes, lungs, skin, eyes, liver, spleen and phalangeal bones. The disease is usually chronic and symptoms vary from an asymptomatic state to the presence of severe respiratory incapacitation or manifestations of an acute febrile illness. The intracutaneous tuberculin test is usually negative. Hyperglobulinemia, leucopenia, hypercalcemia and elevated alkaline phosphatase may occur.

A variety of more specific disease entities may simulate the clinical and histological manifestations of the disease.

Members of the Connecticut State Medical Society reading papers before other organizations are requested to submit their papers to the JOURNAL for consideration by the Board of Editors for publication. Please send them to:

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CONNECTICUT MEDICINE
160 St. Ronan Street
New Haven, Connecticut 06511

THE PRESIDENT'S PAGE

AMA INTERIM SESSION

The 1969 Semi-Annual Meeting of the American Medical Association was held in Denver, Colorado from November 24th through December 4th. Aside from the excellent attendance of approximately 5,000 physician members representing all 50 states, territories and all types of medical practice, there were another 1,500 consisting of exhibitors, AMA field representatives, wives, guests from foreign lands, residents, interns and medical students. Several sections held scientific programs and there were over 100 scientific and commercial exhibits. One cannot help but wonder *why* so many physicians would interrupt a holiday (Thanksgiving) weekend, delay Christmas shopping and other preparations and, above all, jeopardize their medical practice. Ask yourself this question, "Why should 5,000 physicians, which included society officers as well as AMA Delegates, sacrifice time, money, energy and, especially, their family love and obligations for the 215,000 members of the AMA—*you* included?" Bluntly speaking, all were there to learn, and to improve their practice. Two hundred forty-two of two hundred forty-four members of the House of Delegates were there also to support your resolutions and to evaluate and act on those from other states.

Representing YOU, against all known forces which may affect your practice and against which you can fight by vote or your own resolution, is just one of the "fringe benefits" of your AMA membership. For the few who still ask themselves the question; "What has the AMA done for me—what am I getting for my dues?", feed and console your minds by reading the superb article by David B. Weihoupt, member of the Division of Public Affairs of the AMA, The Viewing Box, July 1969, p. 659-665. If you are not convinced—write me. The advantages of AMA membership are many and varied. Admittedly these advantages are not received by the members in *one* package upon payment of dues but rather "on a piece-meal basis of letters, pamphlets and literature, etc." throughout the year.

A. *Basic Facts*

1. Of the 317,000 physicians in this country, only 215,000 are AMA members. Of these only 164,000 are dues-paying; the others are exempt from dues, all or in part.
2. Twenty-eight percent of the AMA's total budget comes from physician dues. The rest comes from advertising and exhibit revenues.
3. It is officially stated that "your dues of $70.00 would have to be over $220.00 to make up needed funds to operate if it were not for the abilities and the hard work of the people at AMA in obtaining these revenues". (referred to above.)
4. The total of 922 employees receive approximately $5 million dollars of the budget for salaries. The employees include physicians, attorneys chemists, journalists, biostatisticians, and accountants of high calibre.
5. The AMA pays approximately $275,000 for real estate taxes and $350,000 for social security payments.

B. *Benefits from AMA Efforts in Publishing*

The AMA is one of the worlds largest publishers and spends approximately $12 million of its budget yearly for paper, printing, and mailing. AMA's publishing efforts entail the following:

1. JAMA, "Today's Health," AMA News—free to all members. The JAMA alone has a total circulation of 219,000. What is not known to the average AMA member is that the 3 publications and specialty journals cost the AMA about $50 per year to mail to each AMA member.
2. The AMA Directory (3 volume set) is published bi-annually and sent to every state and county medical society, all journal editors and libraries of 94 medical schools. The biographical and educational data on every licensed physician in the U.S.A. is contained therein.
3. It is estimated that over 3,500 different pamphlets on child care, health education, health tips, sex education etc., are sent out yearly in answer to over 100,000 requests for each.
4. Two million copies of AMA First-Aid Manual have been sent out, upon request, during the past several years.
5. "Horizons Unlimited" on health careers has been mailed by the tens of thousands, free of charge, to schools, colleges, and medical societies.
6. Thousands of manuscripts are reviewed annually.
7. "Winning Ways with Patients" was mailed out free in 1967—a total of 25,000 copies.

And many more. Suffice it to say, the gigantic publishing effort of AMA was undertaken to inform and educate *YOU,* the hundreds of schools, allied health professions and institutions and county and state medical societies. In addition, thousands of printed commentaries are mailed annually on legislation, state laws, federal laws, plans and programs of the AMA, in addition to the normal replies to everyday component society organizations.

C. *Requests for AMA Aid*

1. Letters (approximately 21,000 pieces of first class mail) are handled *daily,* covering countless numbers of subjects.
2. Frequently AMA receives 1,000 long distance phone calls per day on matters medical—some of them emergencies.
3. Annually, some 30,000 requests for help are received from the public as well as many thousands from physicians.
4. The Archives of the AMA takes care of a prodigious amount of requests monthly. Some are:
    a. 2,400 research requests
    b. 750 requests for books
    c. 40,000 books in library on loan
    d. Requests for one or more of the 500 films in the library.
5. Film on "Medical Careers" has been shown 90,000 times. The one entitled "Careers Unlimited" has been shown ¼ million times.
6. For the future, the AMA hopes to initiate a program "Report of the Nation" a coast to coast 1 hour T.V. program, 3 to 4 times a year.

D. *Other AMA Activities*

1. Organizaiton, timing, etc. of approximately 1,000 meetings/year with 800 physicians serving without pay on 80 commissions, councils and committees. The work concerned with Medical Quackery and Research on Tobacco and Health alone was a stupendous effort.
2. Annually, some 400 scientific lectures and 400 exhibits are arranged for AMA members.

3. AMA-ERF Briefly, in the past few years, 45 million dollars in loans, including 28,000 separate loans to 19,000 medical students, interns, and residents have been arranged.
4. The Law Division of the AMA is one of the most active, supplying to the AMA members throughout the country countless numbers of legal opinions, guidance, information on medical liability, taxation, insurance, libel, slander, etc.

Space will not permit me (let alone our gracious editor, Dr. Louis Nahum) to enumerate further activities of the AMA that, directly or indirectly, affect YOU and your practice. One could perhaps mention the successful effort of the American Medical Political Action Committee, the Washington Lobby, the Public Affairs Division. Suffice it to say, "in union there is strength," and your membership in the AMA provides you with many advantages enumerated above. How can you miss?

The entire day prior to the opening of the Semi-Annual Meeting last month was devoted to a full, detailed, and frank discussion of "Peer Review." The program was exceptionally well attended and considered instructive by most. It was comforting, however, for those of us from Connecticut to note that most of the fundamental principles, methods and results of the "Peer Review" were, in great measure, already well known and fully appreciated here.

The formal meeting of the House of Delegates was convened at 2 p.m. Sunday, November 30th. A total of 242 of a maximum of 244 delegates were seated ready to consider 60 resolutions and dozens of reports. Following the prescribed format, 10 reference committees went into session, some of which appeared like the feverish hours before a presidential election—hectic, wide-open, brutally frank but maintaining decorum. All of this represented a fight for YOU, and your practice. It would be presumptuous of me to present the actions of the House of Delegates. This will be done, in great detail by our Delegates, who performed commendably both at the New England States breakfast sessions and also at the meetings of the Reference Committees. However, by the same token, I would be remiss in my duty if I did not inform you at this early date of the following actions (3) taken by the AMA House of Delegates. Briefly they are:

1. *Connecticut Resolution Concerning Cost Control of Hospital Services.* At the Semi-Annual Meeting of our own Society, on December 11, the Chairman of the Council reported on this resolution of the Council and the subsequent meeting with representatives of the Connecticut Hospital Association. In Denver at the packed session of Reference Committee D, considerable discussion took place, ending with only one dissenting vote in the audience. Perhaps surprising to some, the President of the American Hospital Association spoke at length but in favor of the resolution. The House of Delegates, after discussing the slightly modified version of the Connecticut original resolution, voted in favor of it. The important resolve is as follows:

   > "Resolved, that the AMA Board of Trustees request the Board of Trustees of the American Hospital Association to join with it in urging hospital boards and hospital medical staffs to develop and initiate cost control measures for hospital care services."

2. *Report of the Committee on Planning and Development*
   Submitted by the Board of Trustees of the AMA

   This 60 page report, containing 57 resolutions along with a Minority Report by a member of the Committee, containing 19 suggestions, taken together, represent not only a monumental effort, considerable soulsearching and perhaps some "crystal ball gazing", but also the most forward step taken by the AMA in decades. Both reports were praised, but the former was also criticised in part as being "derogatory, inflammatory and incorrect". The main report was vast in scope and covered a variety of areas, only a *few* of which are listed below:

a. The need for new and improved methods of delivery of health services.

b. Definition of Health—"Health is a state of complete, physical mental and social well-being and not merely the absence of disease and infirmity.

c. Necessity to understand the public's attitude toward government and toward social programs supported by tax funds.

d. Effects on Health Care and Implications for the Medical Profession of Recent Legislation (P.L. 89-97-P.L. 89-289, P.L. 89-749.)

e. Shortages in *all* categories of Health Services; specifically, the *absolute* shortage of physicians.

f. Medical Society Negotiations of Conditions, Regulations, and Fees in Government Programs.

g. Cost Control of Health Care: Utilization and Monitoring of Professional Fees.

h. Hospital Bed Shortages: Utilization, and Hospital—Physician Relationships.

i. Effect of Medicare and Medicaid on Voluntary Health Insurance.

j. Summary of Probable Future Environment.

k. Legislation: Essential Conditions for Successful Public Relations and Legislative Programs.

l. Structure of the Association: The Board of Trustees, House of Delegates, the President, Executive Staff, etc.

m. Academy of the Professions, and the foundation of the "National Academy of the Health Professions for Research and Policy."

As might well be expected, the discussion of this item (2) at the Reference Committee, was long and comprehensive. Much "smoke" was apparently cleared for, surprisingly enough, the House of Delegates considered this subject in an orderly, constructive manner with decorum. The following significant decisions were made by the House of Delegates:

1. The Report of the Committee on Planning and Development and the Minority Report are to be considered on the same basis.

2. The House of Delegates established the policy that a permanent Committee on Long Range Planning and Development be appointed.

3. The House revised the recommendation of the Reference Committee and approved the appointment of an Ad Hoc Committee of 9 members—consisting of 1 from the Board of Trustees, 5 from the House of Delegates, 2 from the AMA at-large and 1 from the Students of AMA (SAMA). This committee was charged with receiving and studying the report of the Committee on Planning and Development and the Minority Report and is to make recommendations to the House of Delegates at the Annual Convention in 1970.

4. Finally, the House approved the recommendation that the main (or Himler) report and the minority report be submitted to and studied by

the component state societies and that their recommendations be submitted to the AMA Headquarters, two weeks before the printing of the Handbook for the House of Delegates—estimated to be May 20th. It is hoped that by such a plan, the Committee and the House of Delegates will have ample time to take appropriate action.

3. *Report of Ad Hoc Committee to Study + Recommend House Action* on Resolution 34 (A-69) (Council on Private Practice)

It will be recalled that the House of Delegates, at the 1969 AMA Annual Convention, referred Resolution 34 (A-69), "Council on Private Practice," to an Ad Hoc Committee for study, recommendations and report to the House of Delegates at the 1969 Clinical Convention in Denver. The two "Resolves" in the Resolution read as follows:

> "*Resolved:* That the American Medical Convention establish a Council on Private Practice, with the primary objective being to espouse the aspirations and goals of private practice, and be it further
> *Resolved:* That medical schools and faculties encourage, by a variety of methods greater emphasis on private practice, greater exposure of students to private practice, greater use of private practitioners in the teaching of medical students, greater use of community hospitals for teaching, and the establishment of residencies in family practice to produce more physicians oriented to the private practice of medicine."

After considerable deliberation, both in the Reference Committee and in the House of Delegates, the latter voted to approve a few changes in the former's report—with the final action being:

> *Resolved:* That the House of Delegates establish a Committee on Private Practice, which committee shall consist of nine active members of the Association and be a Standing Committee of the Council of Medical Service. The functions of the Commitee on Private Practice shall be:
>
> "1. To encourage and promote the private practice of medicine;
> 2. To develop new methods that will promote the private practice of medicine throughout medical school, graduate, and postgraduate training;
> 3. To assist the private practitioner to improve his method of providing medical care continually, including business practices and the efficient utilization of allied health personnel;
> 4. To publicize to patients the merits of private practice;
> 5. To encourage and assist the development of similar committees by state medical associations; and
> 6. To maintain constant liaison with other committees and councils of the AMA to achieve these objectives."

The impact of all actions of the House of Delegates on the practice of medicine is difficult to evaluate at this moment. However, no one will deny the fact, that all members of the House, Reference Committees and others attending the Interim Session, were genuinely concerned with improving methods of delivery of health service to our people and in protecting the noble goals of the medical profession.

Stevens J. Martin, M.D.

FROM THE EXECUTIVE DIRECTOR'S OFFICE

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Peter F. Villano
Director of Public Relations

Josephine P. Lindquist
Associate Executive Director

SUMMARY OF ACTIONS COUNCIL MEETING

Wednesday, November 19, 1969

I. ATTENDANCE

Present in addition to the Chairman, Dr. S. J. Martin, were: Drs. Granoff, Weber, Jr., Edson, Brandon, Abbot, Dean, Gardner, Fabro, Polivy, Rogol, Cramer, Harwood, Petrie, Wilson, Jr., Purnell, Roch, Grant, Nemoitin, Friedberg, Johnson, Gorin, Pelz, Root, Jr. and vonGlahn.

Also present were: Mrs. Lindquist, Dr. Redlich (Yale), Dr. Patterson (UConn), Dr. Hess (Welfare Department), Mr. Donelan (AMA), Mr. Villano and Dr. Richards. Absent were: Drs. Gallo, McDonald, Palomba and Klare.

II. ROUTINE BUSINESS

Approval of Minutes

As printed and distributed, it was VOTED to approve the minutes of the meeting of October 9, 1969.

Resignations, Appointments, Etc.

(a) *Committee on Public Relations*: It was VOTED to accept, with regret, the resignation of Howard F. Root, New Britain, as an at-large member of this Committee, and it was further VOTED to appoint Joseph C. Czarsty, Oakville, as an at-large member of the Committee, replacing Dr. Root.

(b) *Committee to Study Perinatal Morbidity and Mortality*: It was VOTED to accept, with regret and thanks for past service, the resignation of Samuel D. Rowley, Hartford, as chairman of this Committee, and it was further VOTED to appoint Jacob Greenblatt, Stamford, as chairman, replacing Dr. Rowley. Dr. Greenblatt is a member of the Committee.

(c) *Committee on Rehabilitation*: It was VOTED to accept, with regret, the resignation of C. Frederick Yeager, Easton, as a member of the Committee, and it was further VOTED to appoint Sung J. Liao, Middlebury, to Committee membership. Dr. Liao is also replacing Dr. Yeager as Administrative Medical Consultant to the State Division of Vocational Rehabilitation.

Date of Next Meeting

The next meeting is to be called by the Chairman at a date and time deemed by him to be appropriate.

III. OLD, NEW AND SPECIAL BUSINESS

Resolutions

The Council acted on a series of resolutions submitted by several sources as follows:

(a) *From NHCMA*: It was VOTED to receive as information four resolutions received from the New Haven County Medical Association. In brief, these: affirmed the principle that there should be greater representation of practicing physicans in the CRMP administrative structure; approved the Council's actions to establish liaison with Connecticut Medical Service, Inc.; approved the actions of the Council directed toward bettering the current Medicaid Program; and enjoined the Society to continue making an educational grant to COMPAC in 1970.

(b) *From NHCMA*: It was VOTED *not* to adopt a resolution received from NHCMA which advocated that the AMA undertake a study of the feasibility of national hospital insurance.

(c) *From NHCMA*: It was VOTED *not* to adopt and to refer back to the New Haven Association a resolution on the subject of patient's free choice of physician and hospital.

(d) *From Morris A. Granoff, New Haven*: It was VOTED to adopt a resolution introduced by Dr. Granoff which called for the Council to bring to the attention of the Governor the disparity in the amounts of payments being made to hospital clinics vs. private practitioners for medical services rendered to Medicaid beneficiaries (1½-2:1), and it was further VOTED to request the President to bring this matter to the Governor's attention in person and to explain to him the Council's intent in adopting the resolution.

(e) *From the Committee on Public Health*: It was VOTED to receive as information a resolution introduced by this Committee which advocated that the Society take all possible and appropriate steps to cooperate with other agencies "to stop the sources of several drugs and compounds that are being used to entice people into their use, causing addiction" and act "to see what physician members can do to prevent further addiction in Connecticut".

It was further VOTED to approve a second resolution introduced by the Committee which placed the Council in support of "a mass immunization program against rubella among children in grades K-1-2-3", and to apprise the Committee on Public Health of this action.

Resolution—Request for Reconsideration

At the meeting of October 9, 1969, the Council adopted, and transmitted to AMA, a resolution on the subject of cost control of hospital services. Subsequently, communications were received from several sources (HCMA Board of Directors, President of the Connecticut Hospital Association, hospital administrators, etc.) all of which expressed criticism and/or disapproval of the resolution adopted and requested reconsideration thereof by the Council and possible withdrawal of the resolution from AMA. Following a full discussion of the points of view expressed in the several communications, and a reading of the text of the resolution, a motion to reconsider was VOTED upon and failed to carry by a substantial margin. A motion to instruct the Society's AMA Delegates to withdraw the resolution from consideration by the AMA House of Delegates was itself withdrawn without vote.

Finally, it was VOTED to direct the President, in consultation with the President of CHA, to arrange forthwith a meeting of CSMS and CHA representatives to discuss the subject resolution, to explain the Council's purpose in adopting it, and to attempt to resolve the differences in points of view expressed by CHA and the other communicants.

Report—Ad Hoc Committee on CSMS-COMPAC Relations

It was VOTED to receive for discussion a report filed by this Ad Hoc Committee which proposed a method by which the Society could cooperate more fully with COMPAC in the area of political *education* for the members of the Society, but would avoid assiduously any financial or administrative involvement in COMPAC affairs which are directed toward political *action*. Following the approval of several amendments to the original report, it was VOTED to approve the report, as amended, and to transmit the report to the House of Delegates with the Council's recommendation that it be approved by the House.

Report—Ad Hoc Committee on Administrative Organization and Planning

In a verbal report, Norman H. Gardner, Committee chairman, informed the Council that active steps are being taken to seek a qualified lay person to be recommended to the Council for employment in the post of Assistant Executive Director. In light of the fact that the present Public Relations Director will terminate his agreement with the Society in the near future, the Committee recommends that decision be deferred, pending further study by the Committee, as to employment of a new PR Director, legal counsel and perhaps other specialized staff personnel.

Report of Fiscal Advisory Committee—1970 Budget

The Council received the proposed budget for fiscal 1970, as prepared by the FAC, and after review of the allocations and recommendations of the Committee with the Treasurer, Dr. Grendon, it was VOTED to approve the budget as presented and to fix annual membership dues for 1970 at $50, and to transmit the budget to the House of Delegates with the Council's recommendation that it be approved as submitted.

Medicaid Developments

It was VOTED to receive as information a number of written and verbal reports concerning recent developments on the Medicaid front. In particular, a reply from the Welfare Department stated that the Council's five-point statement on billing procedures could not be recognized by the Department, and that the requirement that physicians list as their "fee" the amount allowed for payment under the fixed schedule would be continued. However, in a later communication from the Professional Policy Committee (Commissioners Donohue and Shapiro) it was acknowledged that the Council's position was correct and that appropriate changes in billing procedures will be undertaken. Also, in response to a call for action on the Medicaid program sent to the Commissioners (letter dated October 20), and pursuant to a November 6 meeting of CSMS representatives with the PPC, the Council was advised by Dr. Polivy that, in effect, the concept of a flexible payment schedule could not be implemented (in the Commissioners' opinion) but that they would welcome the advice of the Liaison Committee with the Welfare Department on improving the present substandard and unsatisfactory fixed schedule. It was VOTED to request Dr. Polivy to arrange forthwith another meeting of his Liaison Committee with the Professional Policy Committee to convey to the Commissioners the Council's opinion that the decision to adhere to a fixed schedule is both unwise and unnecessary, and to urge its reconsideration; to offer assistance in revising the structure of the present fixed schedule, but to decline to "negotiate" dollar amounts of payments or to "approve" such payments; and to offer assistance, if needed, to change the current billing procedures to eliminate the requirement that the physician list as his "fee" (on the claim form) the amount that the fixed schedule will allow for payment.

Having been apprised of Commissioner Bernard Shapiro's resignation from his post in the Welfare Department, it was VOTED to adopt a resolution on his retirement, the "RESOLVE" of which reads as follows:

RESOLVED: That the Council of the Connecticut State Medical Society make public note of its high regard for retiring Welfare Commissioner Bernard Shapiro; commend him for the contributions he has made toward bettering the quality and amount of medical assistance available to the underprivileged of Connecticut; express appreciation to him for his willingness to work in partnership with the medical profession in seeking to establish an effective Medicaid Program in our state and to sustain it for the benefit of the needy; and wish him well in whatever future undertaking offers opportunity for utilization of his humanitarian principles and professional competence.

It was further VOTED to present to Commissioner Shapiro an "Award for CSMS Service" certificate, suitably inscribed, and to invite him to attend the meeting of the House of Delegates on December 11, 1969, to receive the certificate in person.

Report—Liaison Committee with Welfare Department

Following acceptance of a report submitted by this Committee, it was VOTED to act on a series of recommendations contained therein as follows:

(1) To approve implementation of a publicity communication to the membership, explaining the physician's role and responsibility in exercising judgment with regard to the need for hospitalization vs. ambulatory care in the treatment of patients; also for judicious prescription writing and judicious ordering of laboratory procedures, and for effective medical practice and concern relating to health care costs.

(2) To refer to legal counsel for opinion the question of taking a legal approach to testing the State's failure to abide by HEW guidelines which call for the levels of payment for physicians' services to be such as to assure the participation in Medicaid of at least two-thirds of practicing physicians, including an equivalent percentage of specialists in each branch of medicine; also, a reducing of services available to beneficiaries as compared to those available in January, 1969.

(3) To pursue with the Professional Policy Committee the need and desirability of revising the present inequitable payment schedule; to institute a "flexible" schedule; to eliminate prior authorization; to provide simpler billing procedures; and to insure prompt payment of claims.

(4) To encourage the Hospital Cost Commission to take prompt action, through the special committee that has been appointed, to recognize for payment the services of physicians rendered to Medicaid beneficiaries in the hospital emergency room setting.

(5) To implement an intensive and continuing public relations campaign which represents the physician as the advocate of consumers (patients) for a uniform, high quality delivery system of health care (including preventive care) for Title XIX patients, with compensation being represented as a secondary consideration but, on a fair and reasonable basis, to be such as to assure broad provider participation in the program.

(6) To table for consideration at the next Council meeting various aspects of the costs of medical education which are currently being charged to patients and to third party payors by hospitals.

(7) To refer to the Ad Hoc Committee on Administrative Organization and Planning, for study and report, a recommendation of the Liaison Committee which "recognized the need for a tight, well-organized State Medical Society-County Medical Association system, with an expanded staff at the State level, to advise and assume delegated responsibilities on behalf of all physicians".

Report—Ad Hoc Committee on Health Care of Poor

It was VOTED to approve three recommendations of the Ad Hoc Committee as follows:

(1) *Definition of the Problem*

Poverty is the root cause of the health care problems of the poor. The Connecticut State Medical Society must be concerned not only with the delivery of medical care but with the other problems associated with poverty: housing, nutrition, hygiene, education, jobs. Tackling these poverty factors with any degree of effectiveness will increase the level of health care for the poor.

Meanwhile, new approaches for reaching the poor must be developed. The physician alone cannot fill the health care needs of the poor. The team approach is suggested with the physician interacting with nurses, specially trained health aides or family health workers, social workers and others. A simple health education program will not do because the poor are not oriented to seeking health care until they are in a crisis situation and, in most cases, lack transportation to the clinic or physician's office.

(2) *Statement of Criteria*

Any health care program set up to meet the needs of the underprivileged, whether in existence or which may be developed and implemented in the future, should embody the following criteria:

- (a) Free choice by the patient of health service providers, including physicians, hospital, etc.
- (b) High quality of services, assured by peer review and evaluation.
- (c) Physician control of policies and practice applicable to the furnishing of medical (physicians') services.

(3) If approved by the Council, the Committee further recommends that the foregoing be publicized widely among the members of the Society, and that the component County Medical Associations and other organized medical groups (city and regional societies) be urged to initiate constructive and cooperative actions within their respective jurisdictions which will lead to meeting the health care problems of the underprivileged in accordance with this "Definition of the Problem" and "Statement of Criteria".

Reports—Committee on National Legislation

It was VOTED (a) to accept, with thanks a report of the Committee on an attached document titled "A Review of the Medicaid Program in Connecticut", prepared by the PR Director in consultation with Dr. Polivy, Dr. Hess, Dr. Richards and others, which is to be mailed widely to national and state legislators, the AMA, etc.; and (b), to receive as information a letter of transmittal accompanying the document written by the Committee chairman, Bernard A. Burnham, Waterbury.

It was further VOTED (c) to approve a committee-drafted resolution, with minor amendments, in support of the AMA's plan for a voluntary national health insurance program, and to forward a copy of the resolution to the President of the American Medical Association and to the Senators and Representatives in Congress from Connecticut, urging the latter's support of the measure.

Resolution—*In Memoriam:* Clyde L. Deming, M.D.

It was VOTED to adopt a resolution memorializing the death of Clyde L. Deming, New Haven; to spread this action prominently upon the minutes of the meeting; and to present a copy of the resolution to his widow and members of his family. The text of the resolution follows:

WHEREAS: Clyde L. Deming, M.D., of New Haven, achieved deserved recognition in Connecticut, nationally and internationally for his outstanding contributions to medicine in his chosen field of urology; and

WHEREAS: He gave most generously of his time and energies to the work of organized medicine both before and after holding the high office of President of the Connecticut State Medical Society; and

WHEREAS: His conduct and bearing as a physician of high principles were exemplary and worthy of emulation by all physicians; and

WHEREAS: He was a friendly and considerate man who stood ready to offer wise counsel unstintingly to all who sought it, whether patient or colleague; therefore be it

RESOLVED: That the Council of the Connecticut State Medical Society note with deep sorrow the passing of a valued friend and esteemed colleague, Clyde L. Deming, M.D., of New Haven.

Connecticut Regional Medical Program

Through the medium of several communications and verbal reports the Council was apprised of recent developments which have bearing on CSMS representation on the CRMP Advisory Board and Executive Committee. Approved by the CRMP Advisory Board, for implementation in January, 1970, is an increase in the Board's membership from 36 to 40, with the number of CSMS-designated physician members remaining at 4; also, an increase in the membership of the CRMP Executive Committee from 7 to 10, with an increase of CSMS designates from 1 to 2. It was VOTED to direct the Chairman to communicate to the Chairman of the CRMP Advisory Board the Council's agreement that the increase in CSMS designates on the Executive Committee is a step in the right direction; the Council's disappointment that no similar increase of CSMS designates on the Advisory Board was approved; and the Council's appreciation of assurance that the structure of the Advisory Board and

Executive Committee will be reviewed annually. Motions to rescind the Council's previous position on "at least one-third" representation on the Advisory Board, and on *not* giving final approval to CRMP until such representation has been realized reasonably, were lost.

For purposes of administration, and on request of CRMP, it was VOTED to request the President, Dr. Martin, to assign, retroactively, terms of office for the four CSMS designates now serving, and, further, to designate a nominee for a three-year term to occupy the one one-year post which will terminate in January, 1970, and to designate two of the four CSMS representatives to serve on the Executive Committee.

Dr. Martin made these assignments as follows:
Incumbents:

Three-year term (1)—Frank K. Abbot, Waterbury
Two-year terms (2)—Carl W. Johnson, Thompsonville; Norman H. Gardner, East Hampton
One-year term (1)—Stevens J. Martin, Hartford
Nominee for Three-year term (1/70)—Stevens J. Martin, Hartford
For Executive Committee (2, 1/70)—Norman H. Gardner, East Hampton; Stevens J. Martin, Hartford

N.B.: *The foregoing is a summary of the proceedings and actions of the Council on November 19, 1969. Detailed minutes of the meeting are on file at 160 St. Ronan St., New Haven, for perusal by any interested member of the Society.*

Placement Wanted

G.P.—desires emergency room position, experienced, age 50, presently in own practice.

SURGEON—38 years of age Board certified interested in a group type practice. Presently in practice. Available immediately.

INTERNIST—32 years of age, Board certified with National Boards, desires full time hospital position in cardiology, will consider partnership. Presently in practice.

OPHTHALMOLOGIST—30 years of age, Board certified with National Boards, interested in an associate type practice.

PATHOLOGIST—32 years of age, Board eligible desires associate practice in Connecticut. Presently in practice, available immediately.

PREVENTIVE MEDICINE—54 years of age, Board certified wishes to associate full-time with college age people. Presently in practice. Would like to give three months notice.

INTERNIST—47 years of age, Board eligible wishes group or associate practice in Connecticut. Military obligation completed in Turkey. Available immediately.

ORTHOPEDICS-EMERGENCY ROOM—30 years of age with National Boards interested in an institutional or industrial type practice. Military obligation completed. Available immediately.

PATHOLOGIST—40 years of age, wishes solo or group practice in Connecticut. Presently in practice with military obligation fulfilled.

UROLOGIST—32 years of age, Board eligible wishes group or associate practice in Connecticut.

GENERAL PRACTICE-EMERGENCY ROOM—37 years of age wishes group or industrial type practice in Connecticut. Available immediately.

PEDIATRICIAN—39 years of age, wishes to practice in Connecticut. Available immediately.

PATHOLOGIST—34 years of age, with National Boards wishes to practice in solo, group or associate type practice in Connecticut. Military obligations completed. Particularly interested in sea shore location. Presently in practice.

SURGERY—35 years of age, eligible with National Boards wishes to practice in solo or associate type practice in Connecticut. Military obligations completed. Presently in practice. Particularly interested in sea shore location. Available immediately.

NEUROLOGY—29 years of age, eligible with National Boards wishes to practice in solo, group or associate type practice in Connecticut.

INTERNIST—38 years of age, Board eligible wishes to practice part time or full time position with hospital as Hematologist in Connecticut. Military obligations completed. Available immediately.

SURGERY—35 years of age, Board eligible wishes to practice in group or associate type practice in Connecticut. Presently in practice. Military obligations completed. Available immediately.

ANYONE INTERESTED IN THE ABOVE IS ASKED TO CONTACT THE PHYSICIANS PLACEMENT SERVICE, 160 ST. RONAN STREET, NEW HAVEN, CONNECTICUT 06511.

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Precautions: Drowsiness, anorexia, slight gastric distress can occur. In excessive drowsiness, consider longer dosage intervals. Persons on full dosage should not operate vehicles. Nonsusceptible organisms may overgrow; treat superinfection appropriately. Treat beta-hemolytic streptococcal infections at least 10 days to help prevent rheumatic fever or acute glomerulonephritis. Tetracycline may form a stable calcium complex in bone-forming tissue and may cause dental staining during tooth development (last half of pregnancy, neonatal period, infancy, early childhood).
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534-9

Electrocardiogram of the Month

Yale-New Haven Hospital
New Haven, Connecticut
Prepared by
HYMAN M. CHERNOFF, M.D.
Associote Professor of Clinicol Medicine,
Yole School of Medicine
Director, Dept. of Electrocordiography
Memoriol Unit, Yole-New Hoven Hospitol

There are a variety of cardiac disorders in which the configuration of the QRS complexes as recorded in the limb leads tend to resemble one another quite closely. However, a careful analysis of the chest leads recorded in each case can lead to the proper diagnosis of the cardiac abnormality present.

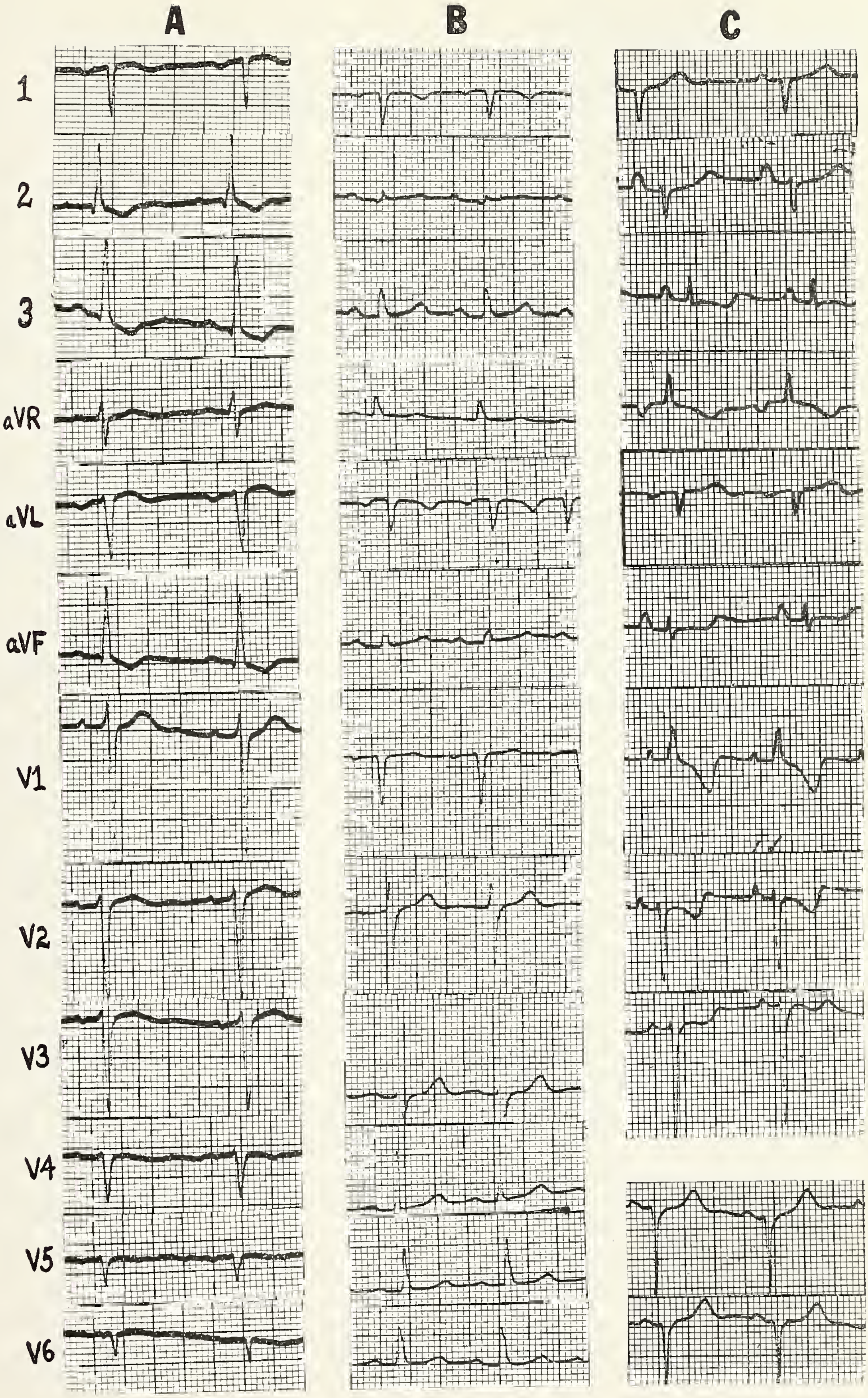
Below are limb and chest leads recorded in three different patients. In each case the mean frontal QRS axis lies markedly to the right. In each case, however, the chest leads exhibit a different sequence of QRS complexes across the precordium from the V1 to the V6 position.

What is the proper electrocardiographic diagnosis in each patient?

Patient A—This tracing was obtained from a patient with Kartagener's Syndrome (dextro-cardia, bronchiectasis and chronic sinusitis). In the presence of dextrocardia the usual electrical relationships are reversed. Thus lead aVR records what normally lead aVL records, and vice versa. The P, QRS, and T deflections in lead 1, therefore, are mirror images of the corresponding deflections in these leads. Leads 2 and 3 are interchanged. The precordial transition is reversed so that leads recorded in the usual fashion over the left precordium record mainly downwardly directed ventricular complexes with the voltage of the R-waves in these leads decreasing progressively from the V1 to V6 position.

Patient B—This patient has no heart disease. The abnormal appearance of the P, QRS, and T complexes in the limb leads is due to a technician's error in applying the limb electrodes. The right and left arm leads have been reversed. This produces in the limb leads patterns similar to those present in dextrocardia. However, careful study of the chest leads reveals the error since these leads exhibit the normal transition of complexes from the V1 to V6 position.

Patient C—This patient has a congenital heart disorder with pulmonic stenosis and interatrial septal defect with resultant marked right ventricular hypertrophy. The limb leads exhibit marked right axis deviation as in patients A and B. However, the P-waves and T-waves are of normal polarity in leads 1 and aVR and aVL (instead of reversed polarity as in true or factitious dextrocardia.) The tall P-waves in leads 2 and VF are consistent with right atrial enlargement. The chest leads exhibit R complexes in lead V1 and rS complexes in leads V2 thru lead V6, findings characteristic of marked hypertrophy of the right ventricle. Comparison of the chest leads in this patient with those of patient A with the dextrocardia reveals that in both conditions the QRS complexes from V2 to V6 are similar in appearance, but that the QRS complexes in lead V1 are markedly different.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By The London Post

British National Health Services

Part 1

Ned Thomas

(EDITOR'S NOTE: Beginning herewith is a series of six reports on various aspects of the British National Health Service—a system for delivering health and medical care to the people of England and Wales. The health delivery system that the English are using is very similar in concept to ones currently in use in Scotland, Northern Ireland, France, Sweden, Yugoslavia, the Soviet Union and a number of other major countries. They are all based on the concept that medical and health care is an inalienable right and not merely a privilege—a principle that is gaining widespread acceptance in most of the developed countries throughout the world. The system may have some relevance for the United States, where some steps have been taken in recent years to provide health and medical care for persons over 65 years of age and for some others under Medicaid and various other prepaid medical plans.)

First in Series

LONDON, England—With pressure mounting in the U.S. for some form of national health insurance, it may be useful to examine England's experience with its National Health Service which has been in existence for more than 21 years.

What lessons, if any, can be learned from them? Is any part of their system of providing free, comprehensive medical and health care for inhabitants of the British Isles applicable and meaningful to the people in the U.S.?

During a recent six week stay in Great Britain we sought answers to questions such as: What has happened to the health of the people of England under the National Health Service? Has it improved or gotten worse?

How has the quality of medicine been affected by it? How have patients generally fared under it? Do they like it? How do doctors like it?

Has it had any effect on the brain drain? Is there any likelihood of its repeal should the Conservative Party gain control of the government in the next election? How much does the National Health Service cost?

To obtain some of these answers we interviewed doctors, a spokesman for the British Medical Association (which is the counterpart of the American Medical Association) a Conservative Party Member of Parliament, an expert on the migration of medical manpower, and lay people.

Firstly, the overwhelming impression that one gets here in practically every quarter is that while there are some obvious deficiencies and shortcomings in the National Health Service, it is here to stay. Another impression is that the vast majority of people here find it satisfactory, want it and would fight for its continuance.

It has found such widespread acceptance here that none of the major political parties want to make an issue of it, and in fact each party is claiming credit for ts establishment and achievements.

As conceived by its architects, the National Health Service Act of 1946 has three main objectives:

1—To ensure that everybody in the country—irrespective of means, age, sex or occupation—should have equal opportunity to benefit from the best and most up-to-date medical and allied services available;

2—To provide for all who want it a comprehensive service covering every branch of medical and allied activity, from care of minor ailments to major medicine and surgery which would include the care of mental as well as physical health, all specialist services, all general services (i.e. by family doctor, dentist, optician, midwife, nurse and health visitor) and all necessary drugs, medicines and a wide range of appliances;

3—To divorce the care of health from questions of personal means or other factors irrelevant to it and thus encourage the obtaining of early advice and the promotion of good health rather than only the treatment of ill health.

We were struck with the fact that in typical English tradition democratic procedures and practices have been worked into the fabric of the National

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MR. NED THOMAS is a science medical writer for the New Haven Register on leave.

Health Service. There is no compulsion about it. Everyone is free to use or not use, as they wish, the health and medical facilities placed at their disposal.

Because of this freedom of action, patients and doctors either acting singly or in concert could have put the National Health Service out of business, if they chose to. The fact that they haven't is an obvious commentary on how they feel about it.

There is a wide latitude of freedom for doctors and patients to move about within the National Health Service or outside of it. Doctors do not have to participate in it if they prefer not to. They can, if they wish, resort to treating private patients only, or they can combine the treatment of Natonal Health Service patients with a private practice.

Patients, on the other hand, have the right to make private arrangements with any doctor of their choice for medical treatment. They are also free to choose their own family doctor under the National Health Service, and family doctors, whom they call general practitioners, are free to decide which patients they will treat.

Doctors are free to treat their patients in their own individual ways, without being subject to any interference in clinical matters.

Furthermore, the traditional doctor-patient relationship has been safeguarded and the family doctor serves as the link between his patients and the hospital and local health authority services which he might need to use.

What has the National Health Service done to the quality of British medicine?

Most authorities agree that the quality of medicine practiced in Great Britain today is equal to the best available anywhere in the world.

British medical specialists compare favorably with the best in the U.S. In fact, requirements for British doctors who want to become specialists or consultants are much more rigorous and more exacting in England than in the U.S.

One measure of how effective the National Health Service has been is to determine what it has done for the health of the British people.

Since it came into effect on July 5, 1948, the number of deaths from communicable diseases in England and Wales has dropped markedly.

In 1950, there were 49 deaths from diphtheria and 734 deaths from acute poliomyelitis, but in 1967 no deaths were attributed to either disease. The number of deaths from respiratory tuberculosis dropped from 14,079 in 1950 to 1,798 in 1967.

Deaths from non-respiratory tuberculosis decreased from 1,890 in 1950 to 245 in 1967, while deaths from measles dropped from 221 to 99, and deaths from whooping cough diminished from 394 to 27 during this same period.

In addition, the number of work days lost by persons infected with tuberculosis between 1951 and 1963 dropped from 27 million to seven million.

In 1967, the infant mortality rate in England and Wales was 18.3 per 1,000 live births, compared to 22.1 in the U.S. Neonatal mortality, which refers to deaths at the time of birth, was 12.5 per 1,000 live births, compared to 16.1 in the U.S.

As of the end of 1967—the last year for which figures are available—more than 49 million persons, accounting for 97 per cent of the people in England and Wales, were enrolled in the National Health Service.

While individual doctors might grumble about the National Health Service, about 99 per cent of the 23,000 general practitioners in England participate in it voluntarily.

In addition to these general practitioners, there are slightly more than 10,000 specialist or consultant doctors in England and Wales, and almost 15,000 junior doctors in British hospitals. Another 10,000 doctors are employed by municipal authorities, universities, industries and other professional bodies.

Of these 60,000 physicians, only 500 to 600, or less than one per cent, limit their work to private patients exclusively.

Many of Great Britain's doctors have some private patients as well as National Health Service patients, but the vast majority of British patients are treated under the National Health Service.

(The second report in the series discusses what benefits British residents are entitled to under the National Health Service.)

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They Call Them the "Fortunate Fours"

A recent five-year study of 28,000 four-year-old children by a team of audiologists at the Mayo Clinic in Rochester, Minnesota, brought to light an incredible fact: as many as one in ten American youngsters begin kindergarten each year handicapped by unrecognized hearing loss. Studies of vision indicate that about 3% to 5% of the nation's children enter school needing eye care.

This does not mean these children are deaf or blind. Most cases of profound blindness and deafness are identified before age four. But for large numbers of children, mild to moderate hearing and vision losses are not recognized until the children receive their routine eye and ear examinations in the second or third grade of school. By this time, hidden damage may be irreparable. Vision development ends at age seven.

Neglect of deficiencies in vision and hearing can be devastating to a child's development. Speech, thought development and normal social relationships depend on normal vision and hearing. Professionals agree that 80% to 85% of learning normally evolves through the channels of vision and hearing. Children with undiagnosed impairments may be emotionally scarred by unwitting school teachers who class them as slow or different when they do not perform on a level with their classmates. The problem becomes critical because a child's first years in school are crucial to his future success.

After spending two years in kindergarten one child in Minneapolis was still in the first grade "on trial" at age eight. His I.Q. was rated at 51. The school nurse was giving him a routine health test and began to wonder if the boy was hearing her instructions. A specialist tested the boy and found a hearing loss of 70 percent in one ear, 28 percent in the other.

The child was given a hearing aid, tutorial help and speech training. Poor hearing had kept him from learning to speak correctly. His I.Q. rating is now over 100. It will take longer to heal the emotional injury he received from his first school years.

An early warning system would have spared this child and thousands like him. Communities have been slow to adopt early testing programs because parents have not realized the necessity for early action.

In Minnesota, thanks in large part to the work of doctors' wives, early detection is a reality. Begun as a pilot project ten years ago in a small surburban village, the Pre-School Medical Survey of Vision and Hearing now serves more than 180 Minnesota communities. With the screening offered them, four-year-olds are given a chance to have hearing and vision defects corrected before they begin formal schooling. The survey calls them the "fortunate fours."

One problem plaguing the hearing screeners at first was the traditional hearing tests, which use the abstract sound of the pure-tone audiometer. The tests require a level of cooperation and response beyond the ability of four-year-olds. Besides, it takes a skilled audiologist up to an hour to get reliable results with a child that age, and there just aren't enough of these specialists to go around.

In 1961 a team of audiologists from the Mayo Clinic, under the direction of otolaryngologist Dr. Kinsey Simonton, came up with the answer when they devised the Verbal Auditory Screen for Children. (VASC). This special audiometer uses words instead of abstract tones and makes a game of the test. With VASC, a lay volunteer can test a four-year-old in five minutes and spot a hearing loss.

The development of VASC was an important step, for it opened the way for non-professional volunteers to operate audiometers and expand the reach of the survey. Under medical supervision, demonstrators are taught to screen for normal vision and hearing. They in turn teach other volunteers to screen. The survey headquarters has developed screening manuals, training films and a package of comprehensive procedures for use by trainees.

The VASC system of screening for hearing consists of a picture chart, an audiometer (modified tape recorder), and two sets of earphones. Twelve objects with two syllable names—fire truck, ice cream, tooth brush—are pictured on the chart. As the child hears an item named through the earphones he points to the pictures. The voice on the tape speaks loudly at first, then decreases in volume. Each ear is tested separately. If a child fails either the eye or the ear test, he may be scheduled for a second screening or directly referred to the family physician.

Physicians report that VASC has proven its accuracy as a screening device in the hands of volunteers. It has recently been employed with decided success in institutions for the mentally retarded. Ninety percent of the medical reports which the survey receives from physicians indicate children referred through the screening actually did have hearing problems and received treatment. In vision referrals, the positive rate is about 80 percent.

"No one who has worked on a survey will minimize the effort involved," says a doctor's wife from Duluth. "But no one who has seen the medical reports on these children, or the look on a mother's face when she learns her child has been rescued from a hearing or vision defect, would ever say that it wasn't well worth the time and effort."

Throughout the ten years of conducting the survey, volunteers give much more than they are asked to give—often against great odds. One screener initiated over 20 surveys during her first few years with the program but "has since lost count." Another volunteer screened 97% of a community's four-year-old children. In rural areas, volunteers fight mud in early spring; snow in late fall. One dedicated demonstrator convinced her husband to take a day off work to drive her through a snow storm to a demonstrator's meeting.

The survey hopes to continue to gain momentum until its goal is reached—screening every Minnesota child, and then perhaps every American child.

The Woman's Auxiliary in Connecticut hopes to start a vision and hearing screening program here in Connecticut next year. We would need the help and support of our doctors. May we hear their suggestions for the program.

Reprint November 1969 MDsS Wife.

Welcome, New Members

New Haven County

Frederick P. Anderson, M.D., 789 Howard Avenue, New Haven, Conn. 06504.
Sandra P. Boltax, M.D., 333 Cedar Street, New Haven, Conn. 06510.
Peter G. Burch, M.D., 477 So. Broad Street, Meriden, Conn. 06450.
Wilfredo E. Cadelina, M.D., 130 Division Street, Derby, Conn. 06418.
Peter Chodoff, M.D., 789 Howard Avenue, New Haven, Conn. 06504.
John M. Christoforo, M.D., Hospital of St. Raphael, New Haven, Conn. 06511.
Nicholas A. Coassin, M.D., 75 New Haven Avenue, Milford, Conn. 06460.
Alan C. Davidson, M.D., 445 New Haven Avenue, Derby, Conn. 06418.
Julio E. De Marchena, M.D., Judd Hill Rd., Middlebury, Conn. 06762.
David M. Dressler, M.D., 34 Park Street, New Haven, Conn. 06508.
Andrew J. Fezza, M.D., 2447 Whitney Avenue, Hamden, Conn. 06518.
James J. Fischer, M.D., 789 Howard Avenue, New Haven, Conn. 06504.
Gerald S. Freedman, M.D., 333 Cedar Street, New Haven, Conn. 06510.
Arthur I. Geltzer, M.D., 333 Cedar Street, New Haven, Conn. 06510.
Robert V. P. Hutter, M.D., 310 Cedar Street, New Haven, Conn. 06510.
Francis J. Kenney, M.D., 1211 W. Main Street, Waterbury, Conn. 06708.
Robert A. Lanzi, M.D., 380 Boston Post Road, Orange, Conn. 06477.
Ira R. Levine, M.D., V.A. Hospital, West Haven, Conn. 06516.
Michael R. Longo, Jr., M.D., 377 Broad Street, Meriden, Conn. 06450.
Richard H. Mattson, M.D., 111 Park Street, New Haven, Conn. 06511.
Stanley E. Matyszewski, M.D., 64 Robbins Street, Waterbury, Conn. 06708.
Melvyn R. Ostrov, M.D., 475 Chase Parkway, Waterbury, Conn. 06708.
Ludwig J. Pavlo, M.D., 121 Wakelee Avenue, Ansonia, Conn. 06401.
Maria M. Pavlo, M.D., 121 Wakelee Avenue, Ansonia, Conn. 06401.
John V. Price, M.D., St. Marys Hospital, Waterbury, Conn. 06706.
Eric A. Sailer, M.D., 186 Sherman Avenue, New Haven, Conn. 06511.
Solomon S. Schwartz, M.D., 789 Howard Avenue, New Haven, Conn. 06504.
Gilbert B. Solitare, M.D., 310 Cedar Street, New Haven, Conn. 06510.
Charles J. Van Der Heide, M.D., 333 Cedar Street, New Haven, Conn. 06510.

Harvey A. Weitzman, M.D., V.A. Hospital, West Haven, Conn. 06516.

Lloyd M. Wilcox, Jr., M.D., 640 Chapel Street, New Haven, Conn. 06511.

Emanuel C. Wolff, M.D., V.A. Hospital, West Haven, Conn. 06516.

Hee R. Yoon, M.D., 2044 Bridgeport Avenue, Milford, Conn. 06460.

Tolland County

Ellen L. Marmer, M.D., 57 Union Street, Rockville, Conn. 06066.

Harold O. Shapiro, M.D., 57 Union Street, Rockville, Conn. 06066.

Windham County

Donald W. Klopp, M.D., RFD #3, Box 783, Gales Ferry, Conn. 06335.

Robert L. Painter, M.D., 168 Main Street, Putnam, Conn. 06260.

Placement Opportunities

DERMATOLOGIST WANTED—Board certified or eligible. Army requirements fulfilled, for association with New Haven Dermatologist with active and growing practice.

GENERAL PHYSICIAN—with interest in psychiatry. Part-time or contract to cover routine hospital services. Nights and/or weekends. For information write or call: Superintendent, Undercliff Mental Health Center, Meriden, Connecticut 06450.

STAFF PSYCHIATRIST—wanted full time or part time to direct therapeutic program in multidisciplinary team. Salary range $18,520-$23,755. Complete tax-free maintenance at nominal costs. For information write or call: Superintendent, Undercliff Mental Health Center, Meriden, Connecticut 06450.

PEDIATRICIAN—needed by small community in eastern Connecticut. Former pediatrician recently withdrew from practice to take fellowship training. Local hospital is well staff with specialists in various fields. Those interested in obtaining further information about this opportunity may contact: Edmond B. Raheb, M.D., Chief, Department of Obstetrics and Gynecology, Day Kimball Hospital, Putnam, Connecticut.

BOARD INTERNIST—for progressive 300-bed Hebrew Home for Aged, Chronic Disease Hospital License application in process, associated with large general hospital, medical school affiliation possible, salary negotiable. Send C.V. to: Benjamin E. Cohen, Chairman, Medical Conference Committee, The Hebrew Home, 615 Tower Avenue, Hartford, Connecticut 06112.

PHYSICIAN who will be willing to work on a salary basis for one or two years with an opportunity for subsequent full partnership after approximately three additional years. Practice consists of general pediatric type practice with the exclusion of obstetrics and major surgery.

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GREAT OPPORTUNITY for Internists, General Practitioners, Otalaryngologist, Psychiatrists and Pediatricians in the Windham area. Solo or group practice available with hospital staff privileges. For further informaton contact: Frank Bird, M.D., Windham Community Memorial Hospital, Mansfield Avenue, Willimantic 06226.

CHEST CLINIC PHYSICIAN—35-hour week. $18,520-$22,846. Excellent fringe benefits. Training available as needed. Contact R. C. Edson, M.D., State Health Department, 79 Elm Street, Hartford, Connecticut 06115.

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VACANCIES FOR PART-TIME PHYSICIANS—Tours of duty are available to provide coverage on our Intermediate (Extended Care) Service evening, nights and weekends. Examples: 5:00 p.m.-8:00 p.m. (Weekdays)-$81.00 per tour; 8:00 a.m.-8:00a.m. (24 hrs. Sat or Sun. or Holidays)-$129.60 per tour. Interested physicians may make arrangements for intermittent or varying part-time tours of duty provided acceptable coverage is maintained during these periods. Part-time tours salary will be prorated according to above rates. Physicians must be U.S. citizens or possess permanent visas, and have licensure in one of the States. Write, visit or telephone: Chief of Staff, Intermediate Service or Personnel Officer Veterans Administration Hospital, West Spring Street, West Haven, Connecticut 06516—933-2561.

VACANCIES FOR FULL-TIME PHYSICIANS— Position open for Physician on Intermediate Service to provide supervision for rehabilitation and extended care for chronically ill patients. Physician must be U.S. Citizen or possess permanent visa, and have licensure in one of the States. Write, visit or telephone: Chief of Staff or Chief, Intermediate Service or Personnel Officer, Veterans Administration Hospital, West Spring Street, West Haven, Connecticut 06516—933-2561.

The Connecticut State Medical Society offers placement assistance through the Physicians Placement Service, 160 St. Ronan Street, New Haven, Connecticut, 06511. This service is for the use of physicians seeking locations, as well as physicians seeking assocates, and is without charge.

ANYONE INTERESTED IN THE ABOVE IS ASKED TO CONTACT THE PHYSICIANS PLACEMENT SERVICE, 160 ST. RONAN ST., NEW HAVEN, CONNECTICUT 06511.

AROUND THE STATE

New Haven County

Board of Governors Meeting
New Haven County Medical Association
December 4, 1969

The Board of Governors of the New Haven County Medical Association under the Chairmanship of President Kurt Pelz met on Thursday, December 4, 1969 at the Colonial House in Hamden. After observing a moment of silent prayer, the passing of Dr. Clyde L. Deming was memorialized by the following Resolution:

WHEREAS: Clyde L. Deming faithfully served the people of New Haven as a practicing urologist for many decades; and

WHEREAS: His knowledge and skill were of such quality as to gain for him national and international recognition; and

WHEREAS: He gave wise counsel and distinguished leadership by example to his colleagues in his participation in organized medicine both before and after his Presidency of the Connecticut State Medical Society; and

WHEREAS: His conduct and carriage as a gentleman and a scholar earned him the respect of his patients and his peers; therefore be it

RESOLVED: That the Board of Governors of the New Haven County Medical Association, in meeting assembled at New Haven, Conn. on the 4th day of December 1969, express its sorrow at the passing of Clyde L. Deming of New Haven; and commit to fond remembrance this fine gentleman by observing a period of silent prayer, and be it further

RESOLVED: That this resolution be prominently spread upon the minutes of this meeting, and that notice thereof be transmitted to his widow and family.

The telegram from H.E.W. warning about the pseudomonas contaminated catheter sets with particular concern about nursing and convalescent homes was read for information.

Our Associate Councilor, Dr. James H. Root, Jr. reported on the Council meeting of November 19, 1969, the minutes of which are published in Connecticut Medicine. Doctor Root described the Council's intention to support a mass immunization program against rubella among children in grades K-1-2-3. He indicated that COMPAC reorganization will be a subject for consideration at the semi-annual meeting of the Conn. State Medical Society House of Delegates being held at the New Haven Medical Association Building on December 11, 1969. The New Haven County Medical Association will be host for that convention. Doctor Root praised the excellency of the 12 page "Review of the Medicaid Program in Connecticut" which was transmitted by Dr. Bernard Burnham, Chairman of the Conn. State Medical Society Committee on National Legislation. He also noted that the Council voted to support the A.M.A. plan for a voluntary national health insurance program.

Dr. Louis Cappucci, Chairman of the New Haven County Public Relations Committee gave a preliminary report on the poll of New Haven County physicians conducted in November 1969. A complete report will be made later.

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The Board of Governors voted to have the Association seek outside professional public relations assistance and a special committee to implement this determination has been appointed by President Kurt Pelz.

The Board, in an effort to enlarge its contact with the membership, and especially the younger members, voted a new policy of having a number of guest members in attendance at each Board of Governors meeting. It was further voted to invite all candidates for election to the Association at any given annual or semi-annual meeting to be invited to attend that meeting.

At the dinner meeting that followed, Dr. John J. Mendillo, Chairman of the Committee on Credentials and Orientation acted as master of ceremonies for the indoctrination of 26 provisory members into active membership.

Respectfully submitted,
William L. West, M.D., Clerk

News From Yale University School of Medicine

The Commonwealth Fund recently announced a grant of $2 million to Yale University School of Medicine for a new and far-reaching attack on the effects of accidental injury—now the leading cause of death in this country in the first half of the normal life span.

The grant will enable Yale's Department of Surgery, headed by Dr. Jack W. Cole, to launch a comprehensive program to improve and reform prevailing patterns and practices for the handling of trauma victims.

The grant will also aid the construction of a major new facility—the Laboratory for Surgery and Obstetrics and Gynecology—to provide a permanent base for the trauma program and house the Department of Surgery. The Fund allocated the grant equally between the start-up costs of the trauma program and the related new facility.

In a statement announcing the grant, Quigg Newton, President of the Fund, said: "The magnitude of accidental injury as a national health problem is underscored in a National Academy of Sciences study which revealed that in 1965 accidents killed 107,000 people in the United States, temporarily disabled ten million, and permanently impaired 400,000. Most of those killed or maimed were under thirty-seven years of age. Thus, aside from the personal tragedy involved, there was a large and irreparable loss to society in productive human talent.

"Although the toll of accidental injury continues to rise, the problem of the accident victim has not yet been approached in a comprehensive way—that is, from the total spectrum of coordinated actions, communications systems, and medical knowledge, techniques, and training required in the care of the patient from the instant of his accident through his treatment and rehabilitation.

"The essential purpose of the Yale trauma program is to pioneer in demonstrating an approach of the kind. Attainment of this objective would place Yale in the forefront of the attack on a grievously neglected national health problem. Moreover, it would exemplify the potential of university medical centers to participate with community institutions and agencies in the task of forging effective and efficient systems of health care.

"In this respect, the trauma program expresses a new order of determination and commitment by the Yale medical faculty and administration to achieve distinction for the University as a prime national center for the advancement of medical learning and care. This commitment, in combination with the urgency and scale of the problem of accidental injury, prompted the Fund's grant for the trauma program—which, it should be added, is one of the largest single grants the Fund has ever made."

Dr. R. John C. Pearson has been appointed associate dean for regional activities and director of the new Office of Regional Activities at the Yale School of Medicine, it was announced recently by Dr. F. C. Redlich, Dean of the medical school.

This office, which was established by an agreement with the Connecticut Regional Medical Program (CRMP), will be responsible for coordinating the regional activities of the medical center as well as providing a liaison with the CRMP and other organizations and agencies concerned with regional medical activities.

Concurrently, Dr. Pearson has been appointed an assistant professor of public health in the health care section and will devote a portion of his time to teaching and research.

Dr Pearson received his B.A. degree in 1951, the Ch.B. in 1954 and the M.B. and M.A. degrees in 1955, all from Cambridge University, England. In 1960 he received a Master of Public Health degree from Yale and that same year was also named field director for the Yale-Middletown (Conn.) oral polio vaccine program under Dr. John R. Paul.

OBITUARY

Morris Tuch, M.D.
1881-1969

Dr. Morris Tuch, one of the oldest practitioners in the State of Connecticut, passed away on October 2, 1969 at the age of 88. He served the health needs of the people of Hartford with compassion and dedication for over 60 years.

During his distinguished medical career Dr. Tuch not only served as a family physician in the true sense of the word, but was also a skilled gynecologist and an excellent obstetrician, who delivered over 4,000 babies.

A native of Europe, Dr. Tuch graduated from Hartford Public High School, completed his premedical studies at Yale and received his medical degree from the New York University Medical School in 1906. He recognized the importance of staying abreast of the advances in medical science by returning to Berlin and Vienna to participate in postgraduate education programs. He further displayed this concern for excellence by spending countless hours in the training of interns and young physicians.

A founder of the Mount Sinai Hospital in Hartford, Dr. Tuch served as president of the hospital's medical staff and was an attending in obstetrics and gynecology at both Mt. Sinai and McCook Hospitals. Dr. Tuch was a member of the American Medical Association, the Hartford County Medical Association and the Connecticut State Medical Society.

Compassionate and dedicated, Morris Tuch was loved by his patients and highly respected by his colleagues. Those of us who had the privilege of knowing this extraordinary man shall miss him. Yet, the legacy he has left us is a great one, and his memory will not soon be forgotton.

David H. Schuman, M.D.

In Memoriam

Beaudry, Joseph Horace, Deerfield Beach, Florida, McGill University 1913. Dr. Beaudry was a general practitioner in the Bridgeport area for many years, before his retirement. He was on the staff of the Park City Hospital in Bridgeport. Dr. Beaudry served in the U.S. Navy as a Lieutenant during American Medical Association, Fairfield County Medical Association, and the Connecticut State Medical Society. Dr. Beaudry died November 12 at the age of 83.

Brown, Abe S., Waterbury, Yale University 1926. World War I. Dr. Beaudry was a member of the Dr. Brown was a pediatrician in the Waterbury area for many years. Dr. Brown was attending Pediatrician at Waterbury Hospital. He was a member of the American Academy of Pediatrics; New England Pediatrics Society, Hezekiah Beardsley Pediatrics Society, American Medical Association, New Haven County Medical Association and the Connecticut State Medical Society. Dr. Brown died December 5 at the age of 67.

Dayton, Arthur B., Hamden, Johns Hopkins 1915. Dr. Dayton was an internist in the Hamden area for many years before his retirement. He was on the staff of the Yale-New Haven Hospital. Dr. Dayton was a member of the The American College of Physicians, the American Medical Association, New Haven County Medical Association and the Connecticut State Medical Society. Dr. Dayon died November 23 at the age of 80.

Deming, Clyde L., New Haven, Yale University Medical School. Dr. Deming was one of the nation's leading urologists. He was formerly chief urologist at the old New Haven Hospital and clinical professor or urology at Yale University Medical School He is credited with helping to discover the efficacy of massive injections of estrogen in the treatment of cancer in the male prostate gland, was the originator of a number of operative techniques, and had done much research work on the various incisions of the kidney. He was a past president of the Connecticut State Medical Society, a member of the New Haven County and New Haven Medical Associations, a Fellow of the American College of Surgeons and of the American Association for advancement of Science. Dr. Deming died November 10 at the age of 84.

Griswold, Matthew H., Berlin, University of Vermont 1913. Former chief of the division of cancer and other chronic diseases of the Connecticut State Health Department and one of the pioneers in the battle against cancer. Dr. Griswold was a private practitioner and health officer for the Town of Berlin and won international repute when he was instrumental in the organization of the Connecticut Tumor Registry. This is a systematic collection of data which now includes extensive information about all the known cancer cases being discovered in Connecticut. He also received a degree in public health at Yale University in 1937. He studied in Vienna for one year. Dr. Griswold joined the State Department of Health in 1936. Dr. Griswold was a member of the American Medical Association, the Hartford County Medical Association and the Connecticut State Medical Society. Dr. Griswold died November 4 at the age of 82.

Siliciano, Raoul A., Bristol, Halmeman Medical School 1924. Dr. Siliciano practiced obstetrics and gynecology in the Bristol area for the past 44 years. He was secretary of the Homeopathic Medical Society for 25 years. He was also a past president of the Medical Staff at Bristol Hospital. Dr. Siliciano was a member of the American Medical Association, the Hartford County Medical Association and the Connecticut State Medical Society. Dr. Siliciano died November 28 at the age of 71.

MEETINGS

GENERAL

May 12, 13, 14

178th Annual Meeting Connecticut State Medical Society

Hartford-Hilton Hotel, Hartford

MEDICINE

Weekly Oncology Courses **12 Noon**

Hospital of St. Raphael, Radiation Therapy Conference Room

January 22

Hodgkin's Disease and Lymphoma: Classification and Clinical Course, David S. Fischer, M.D.; Pathology, Old and New, Bernard Mann, M.D.

January 29

Hodgkin's Disease and Lymphoma: Radiation Therapy, Wayne P. Whitcombe, M.D.

February 5

Hodgkin's Disease and Lymphoma: Chemotherapy, Robert P. Zanes, Jr., M.D.

Peter Bent Brigham Postgraduate Medical Series

February 13 **8:30 A.M.-5:30 P.M.**

Current Status of Antibiotics and Management of Infection, Thomas O'Brien, Director, Microbiology and Infectious Diseases

SURGERY

January 15

Annual Meeting, Connecticut Chapter, American College of Surgeons

Park Plaza Hotel, New Haven

Panel on Surgical Education and Training, beginning at 3:30 P.M., followed by a business meeting; social hour and dinner in the evening.

Contact Francis M. Hall, M.D., 140 Woodland Street, Hartford

March 7

11th Annual Postgraduate Anesthesia Seminar New Jersey State Society of Anesthesiologists

Cherry Hill Inn, Cherry Hill, N.J.

Registration fee (including luncheon) $14.00 to non-members; interns and anesthesiology residents admitted free

May 6, 7, 8

43 Annual New York Eye and Ear Infirmary Clinical Conference

Biltmore Hotel, New York City

Held in conjunction with the 150th Anniversary celebration of the New York Eye and Ear Infirmary. An open house will be held at the New York Eye and Ear Infirmary on Saturday, May 9, featuring scientific exhibits and demonstrations of newer instrumentation and techniques.

Contact Jane Stark, Executive Secretary, 310 East 14th Street, New York, N.Y. 10003

Self-Employed Physicians Now Insured For Disability Under Social Security

Many self-employed physicians reached an important social security landmark. With their earnings covered since 1965, they have now contributed to social security long enough to be insured for disability.

Social security disability benefits can be paid to an insured person under 65 who has a physical or mental impairment so severe as to keep him from doing any substantial work for a year or longer. Payments begin after a waiting period of 6 full calendar months.

Benefits can be as much as $218 a month for a disabled person alone and up to $434.40 a month for a family. Self-employed physicians disabled in the immediate future, however, would probably not be eligible yet for these maximums since their earnings have been covered by social security for a relatively short time. Benefits are figured from a person's average covered earnings over a period of years.

"This disability protection can be a valuable supplement to the physician's private insurance," said Bernard Popick, director of social security's disability program. "It is part of the total social security package of protection-disability, retirement, survivors and health insurance-toward which the physician has been contributing."

Science News

Starvation: Weapon Of Warfare

(Paul O. Okonkwo: *Science*, 165: 753, August 22, 1969) Winick and Rosso have also recently associated malnutrition with inadequate brain development. Current reports from Biafra where great numbers of people, especially pregnant mothers and children, have been deprived of adequate protein and mineral nutrition for two years seem to confirm the observation of Winick and Rosso. The reports are that four babies out of ten born in maternities in Biafra are deformed.

This would seem to indicate that severe prenatal malnutrition can induce small fetal brain size as well as severe skeletal and muscular malformation. Such findings are needed to educate governments of the inherent dangers of malnutrition whether it is in the ghettoes. in Appalachia, in Mississippi or in Biafra.

It would appear that future generations are equally threatened if starvation becomes a legalized weapon of warfare.—L.H.N.

Vitamin Deficit Hurts Fetal Mice

(*JAMA*, 209: 1990, September 29, 1969) Dr. F. Clarke Fraser of Montreal has reported that blocking utilization of nicotinamide for only two hours during gestation in mice leads to a wide array of defects. At seven and one-half days gestation, such deprivation causes malformation of the forelimbs. If the procedure is done on the eighth day the hind limbs as well as the central nervous system are affected.

This drastic and dramatic effect is achieved by giving the animals a single dose of an analog of nicotinamide, which the embryonic cells take up. At the end of two hours nicotinamide is given in very large doses but it is already too late to undo the damaging effect of even two hours of deprivation.

Such studies have not been done on humans and it is not known whether the analog is itself toxic. However, if human embryos should lack key nutrients, this deprivation should produce results similar to those in mice and probably sooner.—L.H.N.

Psychologists Study How We Learn

(*Science*, 223: 563, August 9, 1969) Research on the stages through which information passes in its preliminary analysis by the brain is one of the growing points of psychology. A typical experiment is when a subject is required to remember a group of up to eight alphanumeric items. He is then presented with similar characters on a screen one at a time. The subject has to press one button if the items are in their well remembered original set and another button if they are not.

It takes longer in all cases to make a decision that an item is not in the remembered set than to discover that it is. The subjects thus always conduct an exhaustive search through the items in memory before reacting.

This type of experiment illustrates well the current activities of many experimenting psychologists. By measuring the time taken to react, or the errors made in various tasks in which subjects have to process infomation, they hope to begin to understand the organization of mechanisms subserving recognition, storage, and decision processes.

As a taste of things to come psychologists are already becoming interested in artificial intelligence. Technology now demands automatic systems which recognize patterns, learn to control complex plant, to sort and retrieve information and conduct conversation with people.

Clearly the brain is still the most sophisticated computer we have. It is as important for the engineers and programmers developing automatic systems to understand what is known about brain function as it is for psychologists not to miss any fundamental new advances in the development of intelligence in non-living systems.—L.H.N.

Soluble, Buffered Aspirin Sought To Eliminate Blood Loss In Stomach

(*JAMA*, 209: 17, July 7, 1969) Evidence is accumulating in a number of laboratories that we have not been using aspirin correctly all these years by taking tablets according to Dr. J. R. Leonards. The aspirin of the future will be a tablet you drop into a glass of water and take after it dissolves. Because aspirin is not easily soluble in cold water the tablet breaks up into small particles in the stomach, which lodge on the stomach mucosa. Since acetylsalycilic acid is a moderately strong acid the locally high concentration can result in damage to the mucosa and blood loss.—L.H.N.

Connecticut Medicine

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The first page should list title, the author (or authors), degrees, hospital positions and any institutional or other credits. References should conform to the usual style of the Journal (listing name and initials of author, title of article, journal, volume number, first and last pages and year), and should be cited numerically in the order in which they appear in the text; the number should be limited to the absolute minimum.

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Ordinary articles should not exceed 3,000 words (approximately 3 printed pages). Under exceptional circumstances only will articles of more than 4,000 words be published.

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Our readers are requested to send in items of news, also *marked* copies of newspapers containing matter of interest to physicians. Letters intended for publication should be marked "For Publication." We shall be glad to know the name of the sender in every instance. All copy should be received one month prior to the expected date of publication.

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Communications should be addressed to Louis H. Nahum, M.D., Editor, Connecticut Medicine, 160 St. Ronan Street, New Haven, Conn. 06511. Telephone 865-0587.

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Glenbrook Laboratories, New York, N.Y.	15
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Connecticut Medicine

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CONTENTS

editorials

A Look Into The Future Of Society 73

The Role Of The Government In Health Care 74

The Family Physician—A New Specialist 76

Reflections On Aggression In Man 80

The Town Driver With Heart Disease Under Different Stresses 81

Can Family Planning Alone Solve The Population Explosion 82

On Interferon And Interferon Inducers 85

Chronic Obstructive Lung Disease 86

Medical Dogma: Diet In Peptic Ulcer 87

The Global Effects Of Environmental Pollution 88

scientific

A Curriculum For Training The Family Physician Of The Future, *Joseph Mignone, M.D.* 91

Hepatic Amebiasis: Current Viewpoints In Diagnosis And Therapy, *Lambros E. Siderides, M.D. and Gerald O. Strauch, M.D.* 96

Scintillation Scanning In A Community Hospital: Part IV, *Chester J. Kay, M.D.* 107

A Methodology For Studying The Emergency Care Of The Trauma Patient: Results Of The Yale Trauma Study, *Kristaps J. Keggi, M.D., Samuel B. Webb, Jr., MPH and Ernest J. Broadbent, B.A.* 107

departments

The President's Page 116

House of Delegates, Summary of Proceedings 118

From The Executive Director's Office 120

Physician's Placement Service 121

Doctor's Office 125

Woman's Auxiliary 134

miscellaneous

Science News 123

X-Ray Of The Month, *Arnold B. Riliance, M.D.* 126

British National Health Services, *Ned Thomas* 128

Laboratory Notes 131

Electrocardiogram Of The Month, *Hyman N. Chernoff, M.D.* 132

Obituary: Eugene M. Blake, M.D. 136

In Memoriam 136

Meetings 137

Around The State 138

New Books Received 139

New Books In Review 140

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Connecticut Medicine

editorials

A Look Into The Future Of Society

Society has undergone many technological changes in the last two decades. There is increased speed of communication, increased speed of data handling, increased energy resources, increased power of weapons, increased ability to control disease, and increased rate of population growth. The world has moved into an age of jet planes, missiles, satellites, nuclear power and nuclear terror. We have computers, service and leisure economy, superhighways, superagriculture, super pharmacy, increasing mass higher education, universal TV, oral contraceptives, environmental pollution, urban crisis. In the process, society has developed many "symptoms" of societal illnesses. Environmental pollution is one, another is the urban crisis. In fact several types of crises may reach the point of explosion in the next decade. Nuclear escalation is one. Famine especially in such countries as India is another, the racial crisis is a third. Inflation is another with the consequence of the struggle by Labor for higher wages. Another one mentioned by Platt is the crisis of administrative legitimacy. There is overloaded administrations from universities, unions, cities, national governments which have led to protest everywhere, refusal to accept decisions handed down by some "central elite."

The student revolution is all over the world. Young people familiar with things from childhood have different expectations of life and concerns than their parents who come from another world. Suburbs and ghettos protest, right as well as left. There are many new sources of collisions and protest. One reason is that our present methods of election and management does not give administrations the skill and capacity they need to handle their complex problems, new burdens and decisions. As a result they become unresponsive and repudiated by large numbers of people. Every day some new distinguished administrator is pressured out of office either by vested interests or protesting constituents.

All this may seem trivial to problems of war and famine. Nevertheless these are also dangerous effects of instabilities on the stability of the whole system. In any crisis today administrators or negotiators may work out a basis of agreement between conflicting groups or nations only to find themselves rejected by their people on one or both sides, who then have no mechanism except to escalate their battles further.

What makes all of our crises still more dangerous is that they are coming on top of each other. Administrators can endure an occasional crisis through working together and getting a new sense of importance and unity. But they are not prepared for multiple crises all at one time as happened in New York City in 1968. There was an Ocean Hill-Brownsville teachers strike and a race strike, a police strike, a garbage strike, a longshoreman strike all within a few days. Then every problem may escalate because the people involved no longer have time to think straight.

THE COVER

SYDENHAM AND CLINICAL MEDICINE

THOMAS SYDENHAM (1642—1689), seventeenth-century London physician, at the bedside of a patient—the only place, he believed, where doctors could learn about disease. Sydenham's plain Puritan costume contrasts markedly with high-fashion raiment worn by his lifelong friend, John Locke, physician-philosopher, who frequently accompanied him on his rounds of patients. Sydenham's honest and straightforward observations, accepted and published in many countries, earned him such posthumous titles as that of the "English Hippocrates," and the "Father of Clinical Medicine in Britain."

When this happens the sense of unity, the common purpose gives way to stubborn partisanship.

In the world at large there are daily local wars, nuclear escalation with enough megatonnage to destroy every living thing on earth. Every few years there are confrontations between nuclear powers, Korea, Laos, Berlin, Suez, Germany, Cuba, Vietnam and much more. MacArthur wanted to use nuclear weapons in Korea, Kennedy almost in Cuba. Chisholm's law holds that if a thing can happen it will. Whether we have 10 years or more, unless we systematically find new large scale solutions we are in the greatest danger of destroying our society, our world and ourselves in any number of different ways, before the end of this century. The real reason, however, for trying to make rational estimates of how much time we have left is not because of their shock value, but because they give us at least a rough idea of how much time we may have for finding and mounting some large scale solutions. The time is short, but not too short to give us a chance that something can be done, but it must be done immediately.

The future depends on what we do and can be made better or worse by intelligent, stupid or selfish action. We must work to increase the probability of our survival through the next decade. For this it will be necessary to make a diagnosis of the etiology of the societal illnesses not just enumeration of the symptoms of the diseases which the crisis represent. This is not to say that attempts to alleviate the symptoms are not warranted. In society as in medicine true solutions must depend on recognizing the symptoms, on establishing the etiology of a disease, on making a diagnosis and then and only then can intelligent steps be taken to cure the illness and prevent recurrences in other individuals. These principles hold as true for societal illness as they do for individual human illness.

There must be better ways of handling of the international and intranational crises, otherwise we may have less than a fifty-fifty chance to reach 1980. Anyone who feels more hopeful about getting past the nightmares of the 70's has only to look beyond them to the monsters of pollution and population rising up. Whether we have 10 years or more, unless we systematically find new large scale solutions to societal illnesses, we are in the greatest danger of destroying our society, our world and ourselves in any number of different ways before the end of the century. A few years afo Leo Szilard estimated the half-life of the human race with respect to nuclear escalation as between 10-20 years. This means now!

At the present time we have over 100 medical schools in this country alone where medical research is advancing and doctors are being trained to treat human illness. Institutions for research into societal illness and training experts to deal with them are urgently required. Then we will have people to help us survive the round of terrible crisis and help to reorder our society so that the crisis will not recur. Then we will have a chance of moving into a world of incredible potentialities for all mankind. But let's be realistic, unless we get through this decade we may never reach such a world.

L.H.N.

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The Role Of The Government In Health Care

Health is prized by the American people and has gradually become involved in the political process. Some of the questions being asked are; how can our profession deliver top quality medical care to the family and the community? Can this nation create a medical care and health care system for everyone? How do we arrange our resources and how does each of us utilize his time and skill so that American medicine can realize its productive potential? Elsewhere in this issue is an on the spot account of the way they are trying to do this in Britain. (page 128).

Health is interwoven with the social, economic and political fabric of the nation. We will be as experts qualified to help making the decisions. Governments action embrace many diverse interests each compelling priority for high stakes of power and resources. The head of political decision process is the budget which of course serves the political process in deciding "who gets what, when and how" The increasing shortage of public funds as a result of inflation and war has raised the need for questioning government programs including those concerned with health.

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medical knowledge, perfecting medical technology and building and operating high class medical institutions. Organizing and delivering health care seems now to be pressing forward also. However, government funds for health care are in constant competition with a host of other desirable programs for human betterment and so it is desirable for us to realize the present scope and cost of health services.

Health care today employs 3,000,000 people at a cost of 53 billion dollars. The federal part of this is 18 billion. When we consider that the total expenditure for war and allied activities such as space, atomic energy and ABM is 130 billion then health activities represent about 10 percent of the total federal budget as against over 60 percent for war. Lewis[1] anticipates that federal expenditures for health will, however, increase.

It is of interest that the federal government has been in the health field since 1798 when the Public Health Service was established to make sure that the merchant seamen received adequate health care. Gradually the government assumed increasing responsibility in the control of communicable diseases. Then in 1930 it began to give grants to states to help them attack specific disease problems. After World War II, the Hill-Burton Act brought the government into a partnership with the states for hospital construction.

The biomedical research explosion in the 1950's brought rapidly growing support of the government from 100 million in 1950 to 1.6 billion today. Clearly the people through their government chose to support a search for ways in which to fight disease and the impairment of health. The demand of the people for health care also grew and out of it came Medicare and Medicaid. Clearly our society has made a commitment to health which is politically and financially irreversible. Moreover, federal assistance has now become as crucial to the support of the health-care establishment as it has been to the research efforts.

Clearly health care has become vast and there are many demands and conflicting loyalties. A national program cannot be easily agreed upon Lewis states. Until now the government has established health programs directed to specific action area and the federal health activities are enormous including over 100 separate health programs. Some are direct health care to veterans, servicemen and their dependents, retired military personnel, hospitals for rehabilitation, vaccination, technical assistance and research and grants for specific diseases. The government supports programs for mental health, child health, migrant health, Indian health and many more.

Now we have the major health service payment programs, such as Medicare and Medicaid. Then the government supports many non-health programs which, however, have important health-care objectives, such as Head Start concerned with entire development of the child including its health. Another is the Office of Economic Opportunity (OEC) to attack poverty.

Then we see that at present federal financial resources are distributed in three broad health categories. One is the provision of health services to various groups of federal beneficiaries and indirectly through financing mechanisms such as Medicare and Medicaid. A second is development of health resources including manpower facilities, improvement in organization and delivery and medical research. A third consists of outlays for the prevention of disease and control of health problems including environmental improvement programs.

Of the total budget HEW has the largest share, Department of Defense and Veterans Administration have health outlays in excess of one billion. Improving organization and delivery which includes regional medical program, OEC and the children's bureau receive a very small proportion of the federal health outlay.

L.H.N.

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The Family Physician — A New Specialist

"A family physician provides medical care within one or more, usually more than one specialty discipline of medicine. He assumes in addition the responsibility for providing continuous and comprehensive care for the individual patient within the family (social) contexture supplying portions of the care himself when appropriate and coordinating portions obtained by referral or consultation."[1] Many of today's physicians are called upon to function in this manner but few have had the educational preparation to do so. How to achieve this purpose is the subject

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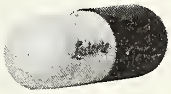

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of the report of the Ad Hoc Committee on Education for Family practice. This committee was set up in 1964 by the Council on Medical Education of the American Medical Association.

Their task was to review present AMA policy regarding the future of family and or general practice and determine whether the goals of such policy are being achieved. They were also to recommend educational approaches by which present goals may be achieved if they are not being achieved. Finally the committee was requested to define and recommend policies by which these goals may be achieved. What was conceived was the need of an American Board of Family practice and how medical students were to be trained to make them competent in such practice. There resulted multiple new undergraduate educational programs which offer the opportunity for medical students to participate in the provision of comprehensive health care. The fact that many medical educators are concerned with bringing this about is convincing indication that the climate is now right for the further development of family practice as a medical specialty.

Many undergraduate family practice programs are barely established and inadequately supported. We as yet have no guarantee that they will receive necessary recognition from their own medical faculties or from potential student participants. As Wilson points out[1] "literally an entire climate of opinion in medical education is yet to be changed and basic faculty attitudes must be further modified before genuine enthusiasm and mutual support for family practice becomes the rule in medical centers."

The initial steps towards this goal must be the development of new models of training for family practice either as an integral part of the medical center or in community hospitals as is being proposed elsewhere in this issue. In medical centers some efforts have been launched but none can be said to have been established on a basis comparable to that of existing specialty services. The medical student, therefore, still does not get a comparable exposure to family practice. Probably major financial support for this purpose when made available will encourage institutions to invest their own resources and the effort of their faculties in this mission. Then positive efforts will be turned to encourage young medical graduates to enter these programs. In order to succeed in this endeavor it is crucial that the status and recognition available through certification by the American Board of Family Practice be made comparable to that provided by Specialty boards of longer standing.

There is a widespread public need for this type of medical service. To make entering this field attractive to the medical graduate, diplomates of this specialty board must be recognized as peers by the already established groups. As an initial contribution two significant innovations in setting standards of excellence have been incorporated into the creation of the American Board of Family Practice. The first is that every board diplomate will be required to demonstrate his competence by passing a carefully designed examination before certification will be permitted. There will be no grandfather clause to permit certification without examination.

The second is that the certification offered will be for a limited period of time and must be earned at regular six year intervals thereafter again by passing suitable examinations designed for this purpose. This reflects the well recognized fact that medical science is advancing at an accelerated tempo with a half-life of knowledge of about six years. A diplomate who has not kept up will be outdated in six years. This fact is as true in other specialties as in family practice and the principle thus established in this specialty may well set an example for other specialty boards.

It appears that there is a very real interest in this movement on the part of the public and also prospective medical students. Many informal polls from both the public and young students indicate a vital interest in the delivery of health care to the family and comparable social units.[1] There thus seems every reason to believe that students will eagerly accept well designed and well presented educational programs in family practice. Of course, besides adequate sources of financial support, such programs will require faculty who are particularly and adequately prepared to provide leadership for family practice programs. Wilson emphasizes that the task will not be easy and will require thoughtful planning, vigorous support and full acceptance by all disciplines.

Medicine as a whole is here being challenged to prove its ability to function as a true profession, to focus on its broad public charge to respond to health needs, those that we know and those yet to be discovered. We certainly have the

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talent, intelligence and intellectual understanding necessary to address the problem. The Council on Medical Education in cooperation with all interested groups will continue to support and coordinate these efforts.

L.H.N.

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Reflections On Aggression In Man

Man is a more aggressive animal than any other primate. At one time the hostility imputed to apes is now judged to have been a mistaken deduction from behavior only seen in zoos. There seem to be three types of aggressive behavior. One is the habitual type which seems to be endogenous and in some way related to personality. Another is that seen in isolated acts of violence which appears to be provoked by particular life situations. In half of the instances of murder as a solitary crime the victim was the wife or girl friend. The third is the type present in all of us. Sigmund Freud[1] believed aggression is an inner drive to oppose libidinal or erotic urges. By developing a conscience or as Freud put it a super-ego, the individual restricts his aggressive expression. He trades hostility for another emotion, the sense of guilt. Psychoanalytic theory holds that the more a person has restricted himself in his capacity to release aggression, the more self-destructively his conscience operates. Guilt proneness in his view is the damage civilized man is called upon to inflict on himself.

Studies in child guidance clinics show that conscience does not develop normally if conditions are not right.[2] Affectionlessness fosters aggression sometimes to a very severe extent. Many aggressive psychopaths have been brought up in institutions or have in other ways lacked affectionate ties with parents. The emotional damage which manifests itself as habitual aggressiveness towards other people is a grave social defect which is extremely resistant to modification. The histories of a particular society influence the personality development of the individual in it and whenever the authority of the past becomes too suddenly and drastically undermined then conduct is likely to become erratic and aggressive.

It appears that working class people tend to be more aggressive than middle class people. They permit hostile behavior in their children and encourage aggression by reacting primitively themselves when a child behaves aggressively. By making use of physical punishment they offer an identification model which is aggressive. Such variation in aggressiveness as due to differences in childhood experiences is shown from a study of nearly 400 mothers.[3] Those who discouraged aggressive behavior, but who at the same time did not punish their children for aggressive acts had the least aggressive children. On the other hand the most aggressive children were those whose mothers permitted aggressive behavior but then punished them for it afterwards.

There is a sex difference in aggressiveness. Men are more aggressive than women. This is true whether one uses as an index crimes of violence, furniture breakage in college residences or scores in psychological testing. The sex difference may be due to innate constitutional determinants. Those who support this position point to the evidence that male sex hormones injected into animals make them more aggressive. Another explanation for the greater aggressiveness of men may be the psychosocial one with a basis of identification. Culturally boys are expected to be more aggressive than girls. Boys seem to need fathers on whom to model themselves. In one investigation boys whose fathers were away at war were found to be less aggressive than boys whose fathers were at home.

Young men are the most aggressive and criminally violent and as we know society makes use of their aggressiveness in war. Under civilian conditions, however, most violent crimes take place in the home and the more serious the violence the more likely is the victim to be closely connected with the assailant. In the home the kitchen is the most dangerous place for men and the bedroom for women.[4] In the majority of crimes of bodily violence the offender has been drinking and often the victim has also.

Aggression is a highly complex response. Man has an inborn capacity to act violently towards other men. If a person is "normal," however, his aggression is modified by life experiences as the individual learns various ways of expressing aggression without anti-social behavior. Some aggressive individuals however Williams[5] points out often show an abnormal electroencephalogram (EEG). He cites other authors who also view habitual aggression as related to abnormalities in the EEG. In the course of 20 years he has obtained EEG's in over 1250 persons (nearly all of them young men) guilty of crimes of violence. He now reports on a quarter of them randomly selected of whom 62 percent were subject to habitual physical aggression or explosive rages.

A distinction emerges between habitual aggression, on the one hand, which seems to be endogenous and in some way related to personality and isolated acts of violence which appear to be provoked by particular life situations. Williams found that those who committed a crime of bodily violence without a background of habitual aggressiveness tended to be older generally and committed only this solitary offense which was usually murder or attempted murder.

The two types of offenders had different EEG's as has also been shown by others. Fifty-seven percent of the habitual aggressives had an abnormal EEG compared with 12 percent of those who committed a single violent crime. This latter figure is close to the rate of the general population. The rate of the EEG abnormality in the habitual aggressives was the same by and large as in temporal lobe epilepsy. The abnormality is thought to be a congenital deviation in early maturation of the brain localized in upper brain stem structures. We must, however, remember that although a disturbance of cerebral function is a major factor in the etiology of abnormal aggression, other factors must also be implicated as well, for nearly half of the habitual aggressives had normal EEG's.

The antisocial behavior is easily recognized but the members of this group differ otherwise in many ways. In some the aggression is associated with mental retardation. In others it is linked with epilepsy, in another with disorder of affect and in still others distortion of social attitudes towards others. Some such individuals ruin themselves and their families by repeated physical violence directed to people, animals or things for little or no apparent cause.

Research to identify the elements of violence and the physiological and psychosocial factors contributing to aggression should be accelerated and experiments with greater explanatory potential should be done. In this way we can achieve better understanding of causes and provide more satisfactory methods of prevention.

L.H.N.

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The Town Driver With Heart Disease Under Different Stresses

If one were to record the electrocardiogram of persons during various types of physical activity, one could determine what happens to the heart rate and also whether evidence of coronary artery insufficiency appear during different stresses. Taggart and associates used a radioelectrocardiograph in persons with apparently normal hearts during driving in busy London traffic in 1967. They found rapid heart rates and abnormal ST-T changes. They now report on a more extended study in a larger number of patients with clinically normal hearts and in persons with different forms of heart disease.

The data were obtained from 78 people, 32 of whom had apparently normal hearts, 24 had coronary artery disease, 4 rheumatic heart disease and one had cardiomyopathy. They also studied 17 racing drivers before and during the race and after the race. Their purpose of including heart disease patients was because driving is thought to be fairly common provocative factor of angina pectoris. They wished to find out whether the drivers heart rates were related to the production of angina and to note the behavior of the ischemic electrocardiogram made during the every day stress of driving.

Taggart had the opportunity to sit along side racing drivers with his radioelectrocardiograph receiver to record some of the responses of the normal heart to excitement and intense competition derived from the effects of physical activity. The instrument they used for the purpose records the electrocardiogram in a convenient and practical way free from cumbersome limb leads. The transmitter is carried by the patient and the receiver and tape recorder is controlled by the operator who sits along side the driver.

In the case of the racers catecholamine in serum were also obtained before and at the end of the race which lasted 20 minutes.

In the racing driver during completion and before the start of the race the heart rate had already risen to 150-180. This rate increased to 180-200 when the race started and remained throughout the 20 minutes of the event. There, of course, was the natural apprehension experienced before and during any competitive event. However, the drivers were not aware of "palpation" is spite of the tachycardia. It is not surprising that their serum catecholamines at the end of the race were raised in all cases and in some being as high as 20 times the resting sample.

The racing drivers were evidently influenced by two main determinants, competition and danger both acting in concert during the race and in an anticipatory sense before the start which raised heart rates to as much at 210. Such rates do occur in athletes during severe exertion such as rowing. It is safe to assume that the tachycardia and the electrocardiogram of driving are determined by emotion similar to that responsible for such changes during angry discussion, discussing problems of personal importance or before examination or after a sudden fright.

In the patients without coronary artery disease a wide variation of in heart rate occurred but most of the ST-T changes could be attributed to the heart rate although in 3 normal the ST-T change was of somewhat greater degree than expected. In the patients with coronary artery disease there was a wide variation in rate also, and ischemic changes occurred in 13 of the 24 while in 6 the change was quite prominent. Five developed multiple ectopic beats while driving and even short series of ventricular tachycardia. Some of the patients were not aware of the tachycardia and the arrhythmia subsided after the drive.

Two patients also had angina as well as the electrocardiographic changes. One developed pulmonary edema during city driving and a second showed early left ventricular failure. Two of the subjects taking digitalis had a rate increase to 170 and 140 respectively, but were unaware of symptoms during the drive. The 4 patients with rheumatic heart disease did quite well. Their heart rates increased from 71 to 90 to a mean maximus of 100. They remained symptom free and developed no new signs in the electrocardiogram. In most of the city drivers the catecholamine levels were not significally altered.

The following factors seemed to influence town drivers both with normal and abnormal hearts: increased awareness of danger, competition to maneuver into the fastest moving traffic lane, aggravation by other drivers, and impatience with delays in dense traffic. One factor not measured is sensitivity of the different drivers and hopefully this can be clarified in a future study.

The incidence of ischemic manifestations was higher than expected. 13 of 24 recorded ischemic patterns. While there is some evidence that syncopal attacks during driving because of the presence of coronary artery disease is an uncommon cause of fatal traffic accidents, there is nevertheless general agreement that persons with active coronary syndromes be advised against driving even in a private capacity. The most obvious one, of course, is Stokes Adams syncope. Anginal attacks provoked by town traffic and or borderline failure resulting from left ventricular disease should also be contraindications to driving a private motor vehicle.

A driver that has coronary heart disease must be given some advice if he is to drive. He must not compete to maneuver into a faster moving lane. He must resist aggravation from other drivers. He must not be impatient with delays in dense traffic. In short drive carefully at all times.

L.H.N.

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Can Family Planning Alone Solve The Population Explosion

There is a population explosion now afoot in almost all countries of the world. Population projections are so often quoted that they no longer startle. It is almost taken for granted that the world population will rise from 3,550 million to something like 6000 million by the year 2000. This is the United Nations median estimate. What is less well understood is that a comparatively stable population such as that of Great Britain will suffer a 24 percent increase from 55 to 68 million in the same period.[1]

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The increase has been sustained over the past quarter century by the world-wide institution of public health programs and the use of insecticides and antibiotics. By tampering with the restraints on human ecology whose classic description is due to Malthus. It is entirely understandable that people should look for a cure to the same source that supplied the cause, namely Science and Technology. It is assumed that new developments in increasing food supply such as utilizing the IR strain of rice will buy time to stabilize population growth with family planning programs. How much confidence can we have in this type of agreement. Do we not here invoke the fallacy of omnipotence of science.

Two distinguished American demographers have recently drawn attention to the fact that such hopefulness rests on a mistaken diagnosis of the problem. The implied assumption of family planning programs is that people would have fewer children than they do if adequate means of contraception were freely available to them. Doubtless this is true to some extent. Nevertheless, the fact remains that the desired family size in countries ranging from the United States to Taiwan is considerably greater than that required for a stable population.

In Taiwan and South Korea where family planning programs are considered as models of what can be achieved by this means, it is hard to be sure that the program has contributed more than marginally to a decline in birth that would have occurred anyway for there is the possibility that family planning programs are largely irrelevant to demographic trends. European countries experienced a decline in birthrate in the 19th century long before family planning was dreamed of. It was a consequence of the industrial revolution and the changing economic and social conditions it brought into play. People had fewer children because they wanted to and the means at hand were demographically effective.

An analysis by Dr. Judith Baker reveals that family size among the poor and uneducated in the United States is not a consequence of this lack of access to family planning advice. The poor actually do have ample access to such advice but have chosen not to take it. The question then arises whether the mere availability of modern contraceptives together with a modicum of mental health propaganda is likely to persuade people to procreate less.

Those who are optimistic about the potential influence of family planning programs appear to neglect the several factors other than the availability of contraceptive technics that determine family size. These include not only traditional and religious attitudes to child bearing but the whole range of social and economic incentives which each society has developed in order to insure its own continuity. The incentives are embodied in the structure of family life, the sanctity of which no political party or regime would publicly challenge.

It appears as though it's the family or at least peoples expectations of the family's role in society that must be altered before the numbers of children traditionally desired is to be reduced. The kind of measures that could be needed include governmental action to deter early marriages, to encourage women to take up careers outside the home as a deliberate alternative to child bearing. It would require abolition of child allowances and other economic incentives to fecundity. It would require further influential sexual mores away from a direction that derives the maximum number of people into fertile union.

Clearly such radial measures are not now potentially feasible in almost all countries of the world. This may be part of the reason for the relative acceptability of family planning programs in almost all countries. These seem to promise a solution in terms of medicine and public health. They are comparatively innocuous to political and most religious sentiments and they permit the impression that something is being done to contain the population explosion without the need for traumatic social changes.

The obstacles in implementing family planning programs are a foretaste for those that will have to face the far more radical measures that may eventually become necessary. Family planning laws and abortion laws are rationalized not because of their effectiveness as demographic tools, but because these sponsors can present them as a means to improve the quality of family life. The development of new methods of contraception such as the "morning after" pill or a pill for men may indeed add some boost to family planning programs in various areas of the world. However, it would be perilous to suppose that such scientific advances can provide a scientific solution to what is essentially a sociological and political problem.

Even though a growing number of countries support or permit family planning activities the fact remains that no government yet has a program to reduce the desired family size. Even if family planning programs were fully successful in their objectives what guarantee is there that the volitional behavior of individual families would lead to containment of the population explosion. It is not naive to hope that individuals can be induced to regulate their family size in the best interests of society by persuasion alone.

In England and Wales the conception rate shoots abruptly upward twice a year during the summer holiday season and in the period between Christmas and New Year. The fluctuations are a demonstration of how social institutions can influence the birth rate. Such seasonal fluctuations in birth rate are a vivid reminder that in these matters at least, people are a law unto themselves and will remain so until otherwise instructed. L.H.N.

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On Interferon And Interferon Inducers

The purification of interferon has turned out to be an almost impossible task. The astounding potency of this substance—as littles as 10-a grams is active—is matched only by the difficulty of purifying it with classical procedures. Nevertheless even for want of the material the potentialities of interferon has not been overlooked.

Two international conferences this year, one in Lyons (Colloquium on Interferon) and the other in New York (Antiviral Substances) testify to the sustained academic and commercial interest in antidotes for viral disease. One of the discoveries holding the greatest promise is that of materials which stimulate the production of interferon in living tissues. The principle is that if one cannot actually inject interferon, its amount can nevertheless be enhanced in situ with the same prophylactic and therapeutic result.

The idea that various polyanions induce interference stemmed from the proposal that foreign RNA elicits interferon production in animal cells, by H. Isaacs the original discoverer of interferon. This was confirmed at the Merck Laboratory by M. R. Hilleman's group with artificial double stranded polyribonucleotide complexes. Now non-biological polymers such as polymethylacrylic acid and copolymers of malic anhydride and divinyl ether have also been found to be active.

The semi synthetic RNA complexes are of particular interest because the mechanism whereby they induce interferon may be related to the way in which virus infection leads to the elaboration of interferon. The story begins with the discovery of antiviral agents in culture filtrates of the fungus Penicillium. A substance named heleninc was isolated from P. funiculosum and another called statalon was obtained from P. stoloniferum. W. J. Kleinschmidt et al then suggested that the active principle in statalon was a virus-like particle present in the fungus and ultimately found that the interferon inducer in this antiviral preparation was viral RNA.

Almost simultaneously E. B. Chain's group at Imperial College, London, in collaboration with M. Hollings et al at the Glasshouse Crops Research Institute, Littlehampton, published a definitive report that the active material is a double-stranded mycophage RNA. Taking this lead several groups have now investigated the therapeutic properties of other double stranded viral RNAs and also synthetic RNAs. These substances have great potentialities, probably even more than the few known double stranded RNA viruses might offer, if only the toxic properties are not a handicap. Toxicity is still a serious problem.

The August issue of Nature, 223, contains three reports documenting the side effects of poly I poly C. Absher and Stinebring (p. 715) present evidence that it is similar to endotoxin in its capacity to stimulate interferon, and in its toxicity. Lindsay et al (p. 717) by studying the pyrogenicity of poly I poly C are seeking evidence to determine whether these inducers exert their effects by inducing synthesis de novo or by causing the release of preformed interferon. At present opinion is divided on this point. It is quite likely that both induction and release occur.

The third article by Adamson and Fabro concerns the embryo toxicity of poly I poly C. The action of interferon stimulators in embryo tissue is of particular relevance to the possible uses of each substance in tumor therapy, since both tumors and embryos represent rapidly growing tissues. H. B. Levy et al and also L. D. Zelezneck and B. K. Bhangan have shown that poly I poly C is effective against tumors in mice and rats and this property is apparently not restricted to viral tumors. But in the viral tumors it is tempting to attribute it to interferon stimulation. I. Gresser's group in Paris have found that interferon itself is potent against viral and non-viral tumors.

If interferon is such a powerful agent against virus and tumors then it is clear why some are pursuing potential therapeutic agents like poly I poly C and why also there is a recent swing in some quarters back to interferon itself even if it is elusive and hard to purify.

L.H.N.

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Chronic Obstructive Lung Disease

It appears from the study of Burrows and Earle[1] that two conditions profoundly influence prognosis in subjects with chronic airways obstruction which is preceded by both emphysema and chronic bronchitis. One is the presence and severity of cor pulmonale especially when complicated by congestive heart failure. The other is severe ventilatory impairment especially with alveolar hypoventilation as measured by increasing hypercapnia.

Most of the features of the disease showed a systematic tendency to worsen although yearly changes were small. Since it is a slowly progressive disorder that begins many years before the onset of clinical symptoms, the question naturally arises as to what if anything can be done to treat or prevent these lethal complications. As far as the advanced groups are concerned, low-flow oxygen intranasally and a thorough program of vigorous bronchial hygiene together with empiric treatment of bronchial infections by tetracycline or amplicillin seems indicated The continuous low-flow oxygen is particularly helpful in patients with congestive heart failure and secondary polycythemia. If there are life-threatening bouts of respiratory failure intensive management in an organized respiratory unit can salvage many of these patients.[2]

It is almost axiomatic that we must be on the lookout to spot emphysema and chronic bronchitis at an early stage before severe airway obstruction supervenes. What we need to know is whether the disease will remain stationary if irritations and infections are removed as we now know that it will progress relentlessly if they are not. Having identified such patients they now need to be taught to live properly and they must be treated vigorously if we are to prevent the downhill course that Burrows and Earle describe.

What the patients must learn as the physician already knows is that a chronic so-called "cigarette cough" and frequent prolonged deep chest infections are the two early reliable indications of a potentially serious disease, chronic bronchitis. From a general health standpoint no one should smoke. Some do get away with it, but it is the smoker with the cigarette cough and prolonged deep chest infection who is not "getting away with it."

There appear to be two types of patients: the predominantly emphysematous (pink-puffer) type of airway obstruction and the "blue-bloater" becomes symptomatic earlier than the "pink-puffer" and also dies five to ten years earlier. Mitchell also emphasizes that in about 25 per cent there is a sudden onset or worsening of dyspnea in the patients for which there is as yet no explanation. A clear understanding of this phenomenon may very well throw new light on the pathogenesis of chronic airways obstruction.

A person who is not yet partially disabled by dyspnea on exertion can however be diagnosed as having early airway obstruction by presence of chronic bronchitis and emphysema. Ventilatory capacity in such patients may decline slowly and over a period of years before the onset of clinical symptoms depending upon the sex, work and living habits of the patients.[1] Patients may lose up to 50 per cent or more of their pulmonary function before they will recognize something is wrong.

The true frequency and severity of anatomic emphysema, at the time of death, is understood in published death rates of emphysema and chronic bronchitis. Mitchell believes the true death rates from those conditions are understated and are probably much higher than is believed.

There have been numerous advances in our knowledge of chronic airways obstruction but more needs to be learned about the pathogenesis of this crippling disease. But even with our present knowledge for such patients if seen when they have only mild disabling or early manifestation of emphysema and chronic bronchitis before the onset of disabling airway obstruction we ought to be able to do a great deal. It requires a high index of suspicion and a very careful look at patients who consult their doctor for other reasons such as annual check-ups. Spirometry especially the single expirogram is advisable in all adults especially smoking men over forty years of age.

Prevention should include abstinence from smoking and bronchial hygiene such as inhalation of nebulized bronchodilatory drug followed by nebulized water or steam.[3] There should be prompt empiric treatment of deep respiratory infections by broad spectrum antibiotics such as tetracycline or ampicillin. Steps are also indicated to prevent such infections by use of influenza vaccines as well as avoidance of close contact with persons having such infections. Mitchell pleads for prevention as being always better than treatment. In virtually no other field of medicine does preventive management give more promise of widespread benefit.

L.H.N.

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Medical Dogma: Diet In Peptic Ulcer

There are two problems in regard to dealing with peptic ulcer patients. One is pain, the other is rate of healing of the lesion. The pain is caused by the hydrochloric acid in the gastric contents. The acid induces a chemical inflammation lowering the pain threshold of the nerve endings in the margin of the ulcer. Vascular engorgement with and without acute inflammation further decreases the threshold for pain. However abnormal motility, hyperperistalis or increased intragastric pressure seems not to be the cause of gastric distress.[1]

There is no conclusive evidence that course or highly seasoned foods retard healing or that a soft diet enhances it. The traditional special diet of milk, pureed vegetables, white meat and fish does not seem to be as valuable in the treatment of peptic ulcer as faith in this time honored method has suggested. Twelve years ago[2] patients eating a normal diet (with the exception of fried foods) or the traditional special diets were shown to be no different with respect to the pain they felt or the extent to which their ulcers healed. However some foods in addition to fried foods do increase discomfort of individual patients and are best avoided. These include seasonings, spices, alcoholic and carbonated beverages, very hot or cold drinks, cabbage, turnips, corn, nuts, sausages and pork. For this reason the diet preferably needs to be adapted to the individual needs.

More recently at the Gastrointestinal Research Unit at the Central Middlesex Hospital in England[2] the effects of normal and special diets on the acidity of the gastric contents have been examined. In general all food buffers and dilutes gastric acid so that acidity decreases. However the special diets have not been found to be any more effective in this respect than a normal diet. All foods and liquids even including water increase gastric secretions. Some like meat, fish and eggs are more stimulating whereas fruits, vegetables and high carbohydrates are less stimulating. However from the work in England these differences do not justify unusual diets.

Patients with duodenal ulcer often complain of pain in the early morning and before meals when the acidity is greatest. The peak acidity before meals has been found to be less when a days diet is given at two hourly intervals than when the same quantity and content of food is given in larger proportions at four hourly intervals. More frequent feeding might therefore be expected to reduce pain during the day although there have been no controlled therapeutic observations of the use of such a diet as yet.

The period of acidity after foods tends to last longer after meals containing a high concentration of protein than after meals with little protein and much carbohydrate and fat. As might therefore be expected, the controlled therapeutic trial at the Unit did not confirm the proposal that a high protein low carbohydrate diet might be useful in the treatment of ulcer. The selection of palatable foods, an intake adequate to maintain normal nutrition, frequent feedings and physical and emotional relaxation at the time of eating are the important considerations.

We must remember that the present standard ulcer diet including milk and cream is high in saturated fats and relatively low in unsaturated fats. Accordingly patients with obesity or with significantly elevated blood lipids or those with a personal family history of coronary artery disease should be on decreased intake of calories perhaps a diet low in saturated and high in unsaturated fatty acids.

The Unit in England is also exploring quicker ways of making a diagnosis. Using the available information about the mechanism of production of symptoms, it has been possible to build up a flow chart algorithmic systems of anaylsis of the causes of symptoms. The patient answers yes or no to various questions and a diagnosis can be made without the use of x-ray or any other examination. The algorithm is in two forms, one for the doctor who questions the patient and one for the patient who answers questions from a book or on a film strip in a modified teaching machine. This version with the machine forms the basis of a system of automated patient interrogation which is being developed by the unit in collaboration with the University of Essex. It should simplify diagnosis and treatment of peptic ulcer.

L.H.N.

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The Global Effects Of Environmental Pollution

Pollution has been defined broadly as "an undesirable change in the physical chemical or biological characteristics of our air, land and water that may or will harmfully affect human life or that of any other desirable species or industrial processes, living conditions or cultural assets; or that may or will waste or deteriorate our raw material resources."[1] Under certain circumstances the natural processes cannot keep pace with the increase of pollutants. Then serious problems arise at first usually on a local scale. On occasion, however, pollution effects may persist, in which case the atmosphere or the ocean circulation may spread them over the whole earth.

One classic example often given and well documented is the rise in the concentration of atmospheric carbon dioxide produced by the intensive burning of fossil fuels during the past few decades.[2] The buffering action of the oceans has not been able to keep up with the increased rate of production and we now find the CO_2. content increased by about 10 per cent and still rising. There is little argument concerning the existence of such an increase, but there is no agreement as to the consequences of this increase on the radiation balance of the earth and therefore on the world climate. However the disagreements will disappear as the CO_2. continues to climb in the atmosphere.

There are now many other examples of world wide effects. Pesticides[3] and lead in the world's oceans, lead compounds in the atmosphere to name a few. Furthermore there may be pollution effects extant which we have not yet recognized or whose consequences we cannot yet ascertain. It is therefore important to examine the situation at frequent intervals to determine whether a pollutant released in our environment could have far-ranging geophysical effects or far-ranging effects in the biosphere and to probe particularly all interconnections in order to expose any weak link in the ecological chain.

We know that global oxygen production depends greatly on photosynthesis including plants and oceanic phytoplankton. Berkner and Marshall pointed out two years ago, if the minute but increasing amounts of pesticides in the ocean affect the phytoplankton, then the world wide oxygen production will be decreased. Most worrisome are the situations in which triggering action sets off a feedback mechanism which preexist in nature. Such feedback mechanisms are believed to be responsible for major changes in the climate and for the production of the Ice Ages. It behoovs us therefore to examine very carefully and even conservatively all pollution effects from human activities.

It is important also that this examination involve scientists from different specialties but with broad interests. Many disciplines must be represented in this examination including geophysics, geology, biochemistry, biology, medicine and of course ecology. The subject matter is vital to the general public, to policy-makers in the government and in the Congress and to all who are concerned about the effects of man's activities on the environment.

A three session symposium on Global Effects of Environmental Pollution just took place at the end of December during the Annual Meeting of the AAAS. Discussed were the world wide effects which may arise from local pollution and the hitherto unsuspected effects which might have serious consequences. One session dealt with the balance of oxygen and of carbon dioxide on the earth's atmosphere and the problems arising from nitrogen compounds in the soil and water on the earth. The global climate effects produced by air pollution and the problem of toxic wastes discharged into the ocean came under scrutiny. There was an assessment made by a panel of the urgency of various pollution problems including a discussion of the public policy aspects.

Problems of environmental pollution are causing increasing concern to many groups both within and outside the government. The AAAS now has a committee on Environmental Quality Problems and there are many private organizations for whom pollution effects are becoming of increasing concern. An outstanding example is the group of scientists which publishes Scientist and Citizen. Becoming alert to world wide effects has led the government of Sweden to call on the U.N. Assembly to conduct a conference on problems of the human environment, and the need for a global network for monitoring environmental quality parameters has been stressed by the International Biological Program.

In setting up the Committee on Envirnmental Alteration the AAAS Board of Directors leaned on a report with some very relevant paragraphs as follows: "Man's relation to the environment is surely one of the most important problems facing society today. Yet these changes are still of limited concern and have been given insufficient attention especially by natural and social scientists.

Improved public understanding is essential, for successful methods of preventing great and perhaps irreversible damage to the environment will often require public financing and public acceptance and may require changes in land or in social customs or institutions."

L.H.N.

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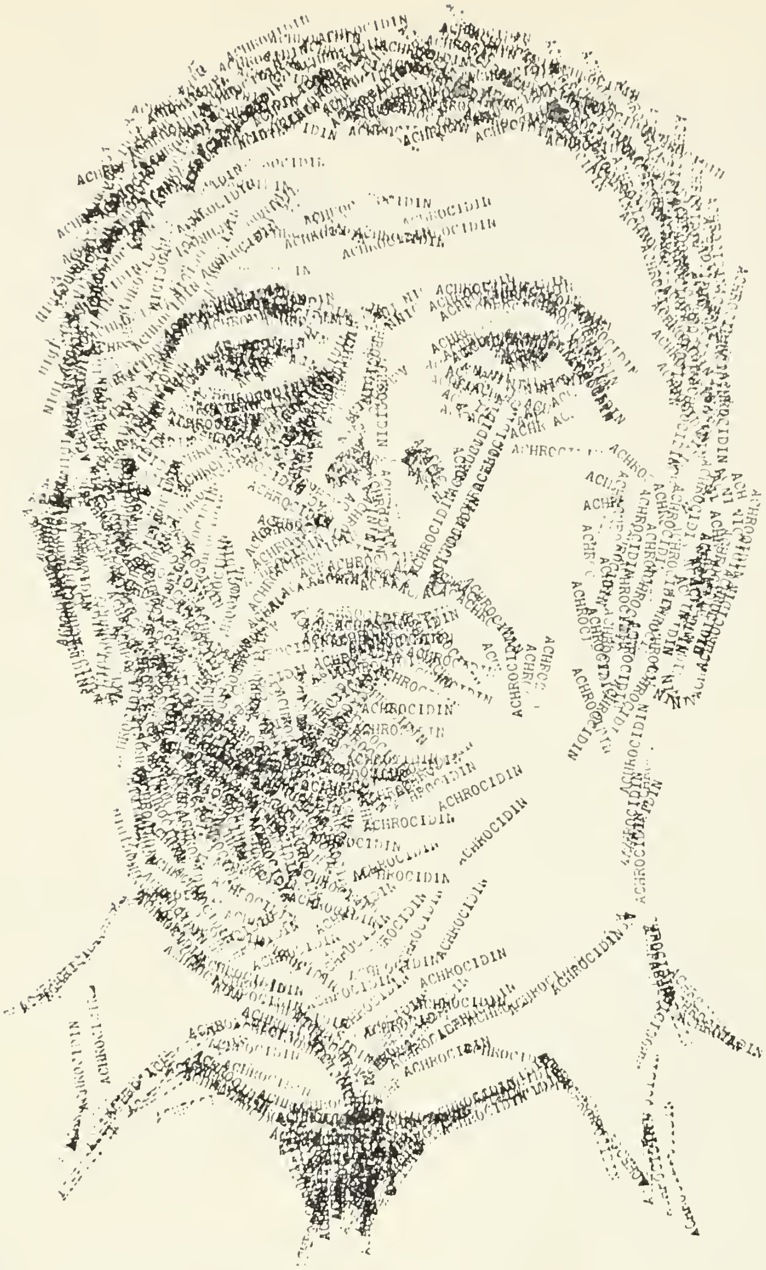

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A Curriculum for Training the Family Physician of the Future

Joseph Mignone, M.D.

It has become increasingly evident recently that the supply of practicing physicians has not kept up with the needs for medical care. Due to the diminishing numbers of family practitioners, and the fact that third party payments, Medicare and Medicaid have made health services available for indigents and elderly who formerly did not have medical care, there has been a growing disproportion between the number of doctors and the number of patients. Several reasons for this have been proposed. One is that very few physicians have gone into general practice. Another is that house officers are better paid than they were two decades ago and they can remain in a residency program for three years and modestly support a family. The present salaries are not great and the physician will not live in luxury, but at least he will survive.

During the past two decades or so, medical schools and many hospitals have been more oriented towards the production of specialists rather than generalists. There is the new status of being a specialist and also the fact that a doctor is certified by a specialty board automatically, in most cases, gives him a staff appointment. This is a status symbol which cannot be looked upon too lightly. Increased income may be a factor in this decision, but is probably not the primary reason.

As a result of the increase in the demands for medical care, the hospital emergency rooms and out-patient departments have been inundated by an ever-increasing number of patients seeking medical advice. It has been well documented that at least 65 per cent of patients who present themselves in an emergency room are not truly emergencies. Such patients go to the emergency room because they have no personal physician and they often present themselves after working hours because it is then that they have the time to seek medical advice. Similarly, out-patient clinics have had an increasing census because these clinics have, in a sense, become the "family physician." Specialization, insufficient numbers of physicians, and the overcrowded clinics have all led to the patients being referred from one clinic to another, a form of fragmentation of care which is unsatisfactory to the patient and an increasing burden on the institution. This fragmentation of medical care could be almost totally corrected if the patient were treated by a well trained family physician.

At this point it might be wise to give some thought about definitions of "family medicine," "general practice," comprehensive care," and "family physicians." These definitions have been well written up in the report of the Ad Hoc Committee on Education for Family Practice of the Council on Medical Education of the American Medical Association,[1] and also by Dr. Lynn Carmichael who has instituted a family practice residency program at The Miami School of Medicine.[2, 3] I accept Dr. Carmichael's definition that "family medicine is that branch of medical science that has as its responsibility, the continuing health maintenance of the family. The general practice of medicine is a form of delivering medical care. It involves the episodic treatment of disease without regard to age, sex or organ systems. The goal is service and there are cultural, political, geographic and economic aspects." On comprehensive care he states, "health concerns can be divided into demands for which the patient seeks care, and needs, or which the individual or family is largely unaware. The degree of 'comprehensiveness' is the extent to which the needs as well as the demands are met."

The family physician is the family health care specialist who, through continuity of care, has developed a tenured relationship with the family. He accepts the family as the unit of care and actively promotes its health. In the past, one could become a family physician through experience gained in the general practice of medicine or pediatrics. While many general practitioners, pediatricians and internists become good family physicians, none have been specifically trained for the role.

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There is both experimentation and controversy as to just how such an individual should be trained. Dr. Richard Weinerman believes in "satellite clinics".[4, 5] I am not in complete accord with the concept of satellite clinics because these are fixed in a community and would remain there while the population changed. It seems to me more practical to have these clinics within or near the community hospital and they would be available to the same population no matter where they lived. Dr. Robert J. Haggerty of the University of Rochester Medical School has encouraged the use of community hospitals in developing the practicing family physician.[6, 7] Because of the need for cooperation of behavioral and biologic sciences, there will be need for a team of social scientists and a physician in addition to others. This is the health team approach. He has stated, "if any part of health services, for instance, is so well proved that it only needs application, it is probably not university's role to provide such care. Especially in the field of delivery of primary health care, we now have so many unanswered questions that the role of the university must be to remain free enough of daily demands for service to be able to inovate, to develop new theories and excite students to carry on development of new ideas in the next generation."

Because of the inadequate number of physicians to give medical care, the Federal Government, medical schools and health educators have been concerned as to how best to provide comprehensive medical care to patients in the future. Dr. Ward Darley, who had been Executive Director of the Association of Medical Colleges from which he retired in 1964, fostered the concept of comprehensive continuing patient care.[8, 9] The Millis Report in 1968 proposed a primary physician, but did not adequately describe who this primary physician should be.[10] The Ad Hoc Committee on Education for Family Practice of the Council on Medical Education of the American Medical Association has come forth with the concept of a "family physician".[1] As a result of the report of this committee and with the strong support of the American Academy of General Practice, in December of 1968 the "Essentials" for Residency Training in Family Practice was approved by the House of Delegates of the American Medical Association at its clinical covention.[11] This residency program is of three years duration following graduation from an approved medical school. The requirements are quite general and several programs have been proposed. Three such programs are as follows:

PROGRAM I

Medicine	33%
Pediatrics	16%
Surgery	16%
Obstetrics-Gynecology	16%
Psychiatry	8%
Community Medicine & Electives	11%

PROGRAM II

Medicine	50%
Pediatrics	16%
Psychiatry	16%
Community Medicine & Electives	18%

PROGRAM III

Medicine	33%
Pediatrics	16%
Psychiatry	16%
Community Medicine & administrative services, including health service administration & electives	35%

Within any of these programs it is essential that family practice be integrated. This would require the continuing care of the certain number of families during the entire three years of the residency program. The remainder of the time would be in supervised training and education, primarily in Medicine, Pediatrics, Psychiatry and Community Medicine, but with sufficient time allowed for electives in any sub-specialty. At the end of the three year residency program an examination would be given by a Board of Family Practice which would be comprehensive in nature, but oriented to a physician who will practice family medicine. The Board which will formulate this examination will consist of five members from the section of General Practice of the American Medical Association; five members from the Academy of General Practice; and five members from the specialty sections of the American Medical Association, namely, Medicine, Pediatrics, Psychiatry, Obstetrics and Gynecology, and Surgery.

As of August 14, 1969 there are twenty approved residency programs for family practice.[12] Many of these are in hospitals affiliated with medical schools. At this time, there have been no gradutes from any residency program and, therefore, it is not possible to judge how effective these residencies will be. On

July 1, 1969 the American Board of Internal Medicine revised its requirements for admission to examination and certification by the Board.[13, 14] The new provisions provide that candidates who have completed a minimum of two full years of post-doctoral education in Internal Medicine will be admitted to a "qualifying examination" provided they are engaged in a third year of post-doctoral education in Internal Medicine or a related field at the time that they undertake that examination. Candidates who are successful in the qualifying examination and have provided evidence that they have completed the required three post-doctoral years of education, will be awarded a certificate attesting to these accomplishments. It is the aim of the Board of Internal Medicine to qualify physicians who are preparing themselves for the practice of Internal Medicine with the goal of serving as a general internist or primary physician. A second certificate will be offered designating as "Diplomates," those who have passed this qualifying examination in Internal Medicine and have completed a minimum of four years of post-doctoral education and have passed an advanced examination. It is the thought of the Board of Internal Medicine that the Diplomates would be the consultants. This type of post-doctoral education is very much like what is now being offered and it has been proven that an insufficient number of practitioners can be developed through this system. It might well be that those who could not pass the certifying examination would become practicing physicians more or less by default, and would not actually have a sufficiently broad training in Psychiatry, Community Medicine, Sociology, etc. to be a true primary physician.

The following is an attempt to set up a Family Practice Residency Program in The Hospital of St. Raphael:

FIRST YEAR

Sixteen weeks Medicine } OR vice versa
Twelve weeks Pediatrics }
These will include experience in O.P.D. and E.R.
Also in sub-specialty clinics such as Cardiology, Hematology, Dermatology, and Medical Chest.
Eight weeks Obs and Gyn including O.P.D.
Eight weeks Surgery including O.P.D. and E.R.
Four weeks Psychiatry
Also one or more days per week throughout the year in a Family Practice Group. Also "on call" for family care.

SECOND YEAR

Sixteen week Medicine } OR vice versa
Twelve weeks Pediatrics }
These will include O.P.D. and E.R. as in first year and/or other sub-specialty clinics such as Oncology, E.N.T. and Psychiatry.
Eight weeks Psychiatry
Four weeks E.R. (Surgery)
Four weeks Obs and Gyn includng O.P.D. and E.R.

Also one or more days per week throughout the year in a Family Practice Group. Also "on call" for family care.

THIRD YEAR

Twenty weeks Medicine } OR vice versa
Sixteen weeks Pediatrics }
Also including O.P.D. in elective services or clinics.
Fourteen weeks Community Medicine and electives here or at Yale.
Fourteen weeks Psychiatry

Also one or more days per week throughout the year in a Family Practice Group. Also "on call" for family care.

This program is flexible and can be altered to suit the physicians needs as long as it is acceptable to the Board of Family Practice. (See Categories of Programs in the "Essentials" for Residency Training in Family Practice.)

A large part of the program would be devoted to continuing medical care. Each resident will be assigned a group of families in his first year of residency and he will follow this group for total medical care during the entire three years of the program. Since we intend to begin with three residents each year and at the end of three years there will be a total of nine residents, this will require "X" number of family groups under the supervision of nine physicians who would, in turn, be under the supervision of our staff physicians, including members of our General Practice section. Each resident would be relieved of his duties within the hospital if any emergency should occur within his family group and when this emergency has been resolved he would then return to his duties in the hospital. Also, each resident would be responsible for continuing the follow-up care of his families in the out-patient department of the hospital.

The time spent in Psychiatry, Community Medicine, Environmental Health and a few other subspecialties will be taught with the cooperation of The Yale Medical School.

At the end of the third year of the residency program, the resident will become eligible to take the examination given by the Board of Family Practice and will be certified as a specialist in Family Practice. He should be qualified to take care of at least 90 per cent of the illnesses within families and he will be taught the usefulness of consultants in the areas in which he is deficient. Also, during the three years he will have been exposed to the team approach of practicing medicine, and he will know how best to utilize psychiatrists, social workers, psychologists and other paramedical personnel. The resident would be the "quarterback" working with such a team and, in a sense, this would be group practice. Several physicians trained in a similar way could form a group to practice medicine and use paramedical personnel to help relieve them of many of the routine duties of physicians, including taking histories, filling out insurance forms, etc. Any graduate from this program who has been certified by the Board of Family Practice should be able to go to any community hospital and set up a similar program. The hope is that enough of the "newer breed" of medical students will be motivated to go into family practice residency programs,[15] and the Deans of medical schools would encourage this rather than discourage it as some have done in the past.

I have communicated with the Deans of all the medical schools in the United States and out of 100 letters sent, 69 replies were received.[16] They were asked what they thought of Family Practice Residency Programs and how many medical graduates might be interested in such programs. About 50% of the deans who answered indicated that anywhere between 5 to 20% of their graduates might so be interested. The remainder felt that less than 5% or none would be interested. A large number of replies stated that they did not know what their graduates were doing once they left the medical school. Nevertheless, such information would be helpful in determining what type of physician should be trained for the future.

The Federal Government has recognized the need for universal pre-paid health insurance. Some sort of a plan would be instituted with federal funds to pay for this insurance for the indigent population. There is a strong undercurrent to abolish the "fee for service" principle and substitute a fixed fee schedule for services rendered. It is thought that under this broad insurance coverage there would be more use of ambulatory services and that the cost of hospitalization would, thereby, be reduced.[17] There has been strong clamor for this also from the labor unions, particularly by Walter Reuther. Dr. Dorman, President of the AMA has stated, "the need for such federally sponsored coverage is obvious. A bill such as the AMA-sponsored one based on a concept on income tax credits should be promptly enacted into law."[18] Obviously we need to be thinking about such an eventuality much more than we have thus far.

Congress is showing an interest in the future practice of medicine as witness Bill H.R. 13063 which is to amend the public health service act to provide grants to develop training in Family Medicine. This bill is now in committee for consideration.[19] Briefly, this bill, if passed, would authorize money for grants to medical schools to assist in meeting the cost of special projects to plan, develop, or establish new programs or modifications of existing programs of education in the field of family medicine, and including the development and equipment of appropriate facilities. It is quite likely that this bill would provide funds for both undergraduate and post-graduate training for the purpose of producing family physicians.

I might state that there has been extensive literature in the past five years or so concerning the best way to deliver health care. There is no unanimity as to how this can be done or should be done. There are many advocates of "satellite clinics" associated with large university hospitals. Others believe that a primary physician should be trained in a community hospital affiliated with a medical center. I personally prefer the latter type of training since I believe it is the role of a medical school to do research in models of medical delivery and to do so in small groups rather than to attempt a larger service function for which they have neither the personnel nor the time.

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A Study Of Family Medicine

. . . the most important concept of the family doctor is that he is the one physician who provides primary and continuing care for all family members. He provides the central unifying focus from which the family can achieve adequate complete care. In the future he must not be the physician with the least amount of formal education, but rather one who is skillfully trained in the prevention, diagnosis and treatment of a variety of illnesses. Training programs must be built on the principles of family care while at the same time allowing sufficient flexibility to prepare the physicians for the large number of potential variations of family medicine. The essence of family medicine is care of the family, something no other specialty provides. Family medicine is the family physician's job. The major problem is making this career attractive rather than changing it. —Gregory J. Riley, Carl R. Wille, and Robert J. Haggerty—*JAMA*, June 23, 1969—Vol. 208, No. 12.

Hepatic Amebiasis: Current Viewpoints in Diagnosis and Therapy

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Synopsis-Abstract

Clinical amebiasis may increase in the Northeast United States because of socioeconomic factors and increased international travel. Recent experience with cases of hepatic amebic abscess is here presented to illustrate that therapy need involve only anti-amebic drugs, in most cases, without resort to abscess aspiration or other surgical maneuvers; this is possible because of newer serodiagnostic techniques, such as indirect hemagglutination, and the advent of hepatic scintillography as a tool for diagnosis and the monitoring of drug therapy. The syndrome of hepatic amebiasis may now be redefined as including 1) an enlarged, tender liver, 2) suggestive hematologic findings, 3) suggestive findings by radiography and liver scan, 4) specific serodiagnostic tests, and 5) response to specific anti-amebic therapy (chloroquine, emetine). Surgical intervention is indicated only in unresponsive cases, when secondary pyogenic infection is present, or in cases of ruptured abscess.

Clinical amebiasis has not proven to be a common disease in community hospitals in the Northeast United States; however, its incidence may rise because of the marked increase in civilian and military national and international travel and the changing socioeconomic factors in this country. Amebic disease is a ubiquitous entity with relatively high incidence in all continents, including North America and Europe. The prevalence in the United States is most commonly stated to be 10 per cent.[1]

The purpose of this paper is to present our recent experience with hepatic amebic abscesses encountered at the Stamford Hospital. Emphasis is placed on the efficacy of current anti-amebic drug therapy, which usually offers the opportunity of complete recovery without the necessity of surgical intervention. Secondly, we wish to stress the importance of hepatic scintillography as a tool in the diagnosis and localization of hepatic abscess as well as for the monitoring of the results of anti-amebic treatment.

CASE I: L. C., a 30-year-old white male, was admitted to the Stamford Hospital on November 18, 1965, with complaints of fever, chills, and pain in the right upper abdomen for three days. Nine months prior to admission, the patient, while in India as an exchange teacher, developed diarrhea. This was thought at first to be bacillary dysentery, but charcoal bodies were subsequently found in the stool by his Indian physician, who made the tentative diagnosis of amebiasis and treated the patient with tetracycline and emetine. Despite treatment his diarrhea persisted for six months. Repeated stool examinations failed to reveal either amebic cysts or trophozoites, but he continued to feel ill. In May of 1965 he was treated for right-sided "pleurisy" in Hong Kong. (Reports of x-rays at that time are not available.) A month prior to admission he began to complain of right upper abdominal pain. A week prior to admission he developed loose bowel movements, fever, and pain in the right anterior lower chest, exacerbated by respiration. Past history was negative except for pneumonia at the age of 5 years and "nephritis" at the age of 6 years. The remainder of the history contained no other pertinent information.

Physical examination revealed a well-developed white male, diaphoretic, with rectal temperature of 39.4 degrees Centigrade. Blood pressure was 120/80 millimeters of mercury. Cardiac examination revealed equality of the aortic and pulmonic second sounds. The liver was palpable 3 centimeters below the right costal margin and was slightly tender. He had definite percussion tenderness over the hepatic area posteriorly, laterally, and anteriorly. The remainder of the physical findings wre within normal limits.

Pertinent laboratory studies on admission revealed the following: Hemoglobin was 14 grams per cent with hematocrit of 40 per cent. White blood cell count was 13,400 per cubic millimeter with normal differential count. Serology was negative. Urinalysis was normal. Fasting blood sugar on admission was 104 milligrams per cent. Blood urea nitrogen was 13 milligrams per cent; serum amylase was 79 Somogyi units; serum glutamic oxalacetic transaminase was 16 units; serum bilirubin was 0.8 milligrams per cent, with 0.2 milligrams per cent direct, and 0.6 milligrams per cent indirect fractions. Thymol turbidity was 2.9 units, and serum glutamic pyruvic transaminase was 18 units; cephalin flocculation was negative. Corrected erythrocyte sedimentation rate was 32 millimeters per hour. Febrile agglutinins were negative. Serum alkaline phosphatase was 14 King-Armstrong units. Repeated blood cultures revealed no growth.

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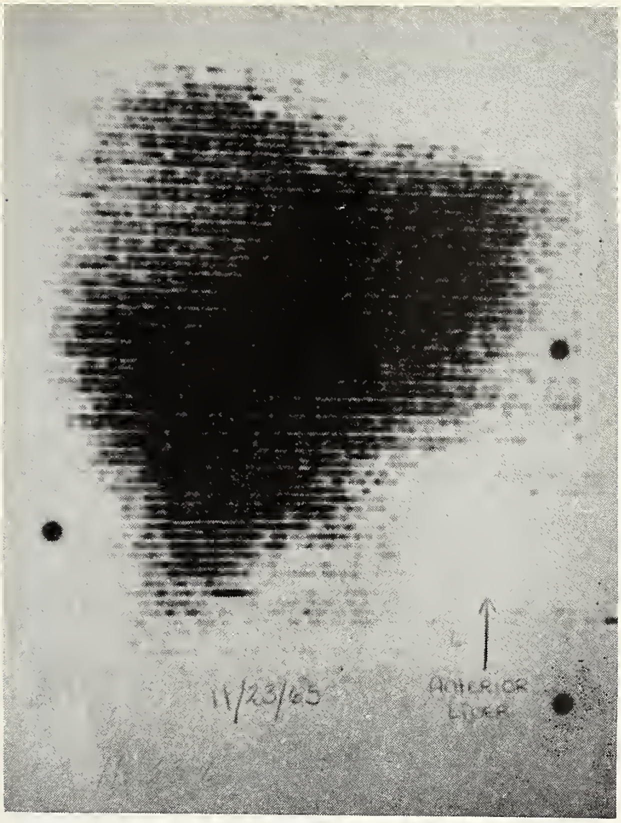

Figure 1

Original anterior liver scan in Case 1. showing hepatomegaly and decreased isotope uptake in hepatic dome due to amebic abscess.

Chest x-ray was unremarkable. Intravenous pyelography was normal. There was questionable visualization of the gallbladder by cholecystography. Barium enema was normal.

The patient's clinical course and laboratory data suggested hepatic amebiasis. His temperature ranged from 36.6 degrees Centigrade to 40.0 degrees Centigrade. Stool examinations demonstrated the presence of cysts and trophozoites of Endamoeba histolytica. Hepatic scan performed on November 22, 1965, (Figure 1.) revealed a large circular area of decreased dye uptake in the dome of right lobe of the liver, and hepatomegaly. He accordingly received the following anti-amebic drugs: emetine, a total of 360 milligrams in six days; chloroquine, 10.5 grams in 21 days; tetracycline, 10 grams in 10 days; and paromomycin, 20 grams in 10 days. Within 48 hours of the initiation of anti-amebic therapy the patient became afebrile, and clinical improvement was sustained throughout his subsequent course.

A repeat liver scan on December 8, 1965, revealed that the area of decreased uptake in the right hepatic lobe had decreased in size, with moderate decrease in liver size. Aspiration of the abcess was undertaken on December 9, 1965; only 10 cubic centimeters of thick, odorless, pink pus containing no amebae was obtained. During the aspiration the patient sustained a small right pneumothorax which was obliterated by a single needle aspiration. During emetine therapy he developed electrocardiographic changes consisting of diphasic and inverted T-waves in Leads 3 and AVF suggesting posterior wall ischemia. Emetine therapy was thus discontinued on the sixth day of treatment. The electrocardiographic changes reverted to normal after the cessation of treatment.

On December 8, 1965, his white blood count was 9,100 per cubic millimeter with normal differential count. Erythrocyte sedimentation rate was 32 millimeters, corrected, subsequently dropping to 2 millimeters. Serum glutamic pyruvic transaminase was 18 units. Total serum protein was 7.5 grams per cent, with albumin of 5.2 grams per cent. Serum glutamic oxalacetic transaminase remained within normal limits, ranging from 14 to 24 units. Indirect hemagglutination test for amebiasis was reported positive on December 18, 1965. The patient was discharged on oral glycobiarsol on December 14, 1965, and has since felt well. Therapy to eradicate his intestinal amebiasis was completed on an out-patient basis. Hepatic scan done on February 16, 1966, (Figure 2.) showed complete healing of the amebic abscess.

COMMENT: This is a typical case of amebic hepatic abscess which developed following incomplete therapy for intestinal amebiasis. The abscess responded well to an anti-amebic regimen, with full clinical recovery and return of hepatic scintillography to normal. In retrospect, aspiration of this abscess could have been omitted, since it was needed neither for diagnosis nor therapy. It is interesting to

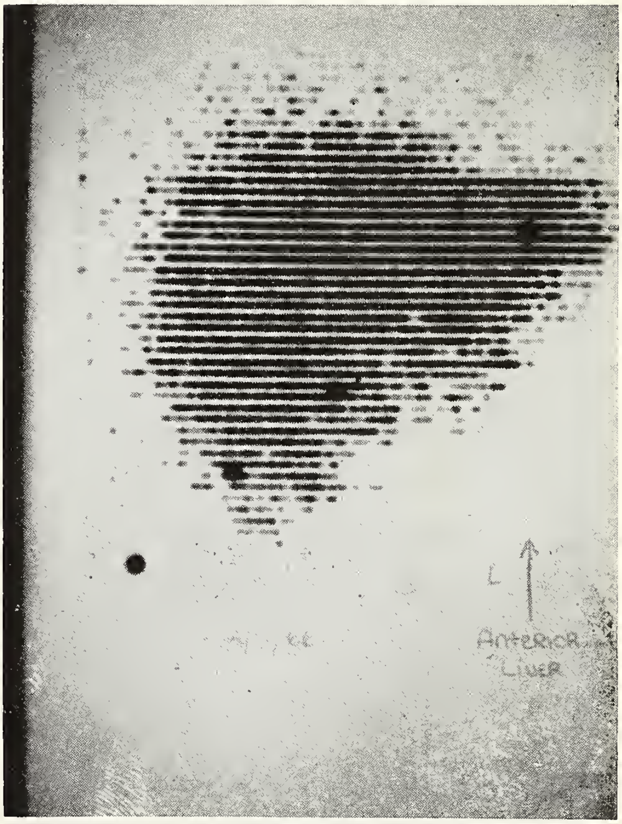

Figure 2

Final anterior liver scan in Case 1. showing return of liver size to normal, and restitution of parenchymal uptake of isotope in hepatic dome following completion of anti-amebic therapy.

speculate whether the episode of pleurisy in the spring of 1966 may have been related to amebic hepatic disease.

CASE II: W. B., a 45-year-old white male, was first admitted to the Stamford Hospital on July 28, 1966, because of vague abdominal pains of one week's duration. This pain, chiefly epigastric, was associated with nausea, anorexia, lethargy, and constipation; it was preceded by four days of diarrhea. For five days prior to admission, fever to 39.4 degrees Centigrade had been present. No jaundice, vomiting, melena, or hematochezia had occurred. The patient admitted to "more than moderate" alcohol intake. No other pertinent history was elicited.

Physical examination revealed temperature of 39.1 degrees Centigrade, pulse of 102 per minute, respirations of 18 per minute, and blood pressure of 130/70 millimeters of mercury. A questionable scleral icteric tinge was noted. Scattered coarse rales were heard over the lung bases. Moderate punch tenderness was elicited over an enlarged liver, which extended two finger-breadths below the right costal margin. The remainder of the physical findings were felt to be within normal limits.

Laboratory studies prior to operation included the following: hemoglobin, 14.4 grams per cent; hematocrit, 45 per cent; white blood count, 17,600 per cubic millimeter with 84 per cent polymorphonuclear leukocytes, 8 per cent lymphocytes, and 8 monocytes; normal urinalysis; serum bilirubin, 1.3 milligrams per cent; fasting blood sugar, 141 milligrams per cent; blood urea nitrogen, 13 milligrams per cent; serum glutamic oxalacetic transaminase, 35 to 56 units; serum alkaline phosphatase, 23 King-Armstrong units; serum sodium, 126 milliequivalents per liter; serum potassium, 4.1 milliequivalents per liter; serum chloride, 91 milliequivalents per liter; serum carbon dioxide content, 17 milliequivalents per liter; serum cholesterol, 160 milligrams per cent, with 53 per cent esterification; serum amylase, 44 Somogyi units; prothrombin time, 14 seconds, with control of 12 seconds; febrile agglutinins, negative; serum calcium, 4.5 milliequivalents per liter.

Electrocardiogram was normal.

Chest x-ray revealed no abnormalities. Oral cholangiography failed to produce gallbladder visualization.

The admitting diagnosis was acute cholecystitis and cholangitis. Antibiotic therapy was instituted, but spiking fever continued unabated. The surgical consultant concurred in the admission diagnosis.

On the fourth hospital day, a mass was palpated in the right upper abdomen. Because the mass was felt to represent a possible cholecystic empyema, laparotomy was undertaken on the same day.

Abdominal exploration revealed "a markedly enlarged, highly congested, soft, mushy liver." The pancreas was thickened and friable. The gallbladder and remaining extrahepatic biliary tree were felt to be normal. The surgeon's diagnosis was acute pancreatitis. Peritoneal fluid was aspirated for amylase determination, a biopsy of omentum was taken, a drain was placed in Morrison's pouch, and the operation was terminated.

Following operation, fever and leukocytosis continued. Six days after operation, thick, pink pus issued from the wound drain site and continued to drain in large amounts. Concomitant with this purulent drainage, fever subsided and the patient's general condition seemed to improve; leukocytosis, however, did not resolve. Sixteen days after operation, the patient was discharged from the hospital.

His course following discharge was marked by persistent drainage of pink pus from the wound, intermittent fever, increasing pallor, and progressive weight loss.

On September 7, 1966, he was readmitted to the hospital.

Pertinent blood studies included the following: hemoglobin, 10.2 grams per cent; hematocrit, 33 per cent; white blood count, 20,700 per cubic millimeter; sedimentation rate, 30 millimeters, corrected; serum sodium, 124 milliequivalents per liter; serum potassium, 4.2 milliequivalents per liter; serum cholride, 86 milliequivalents per liter; carbon dioxide content, 28 milliequivalents per liter; serum bilirubin, 0.7 milligrams per cent; serum alkaline phosphatase, 23 King-Armstrong units; thymol turbidity, 2.2 units; serum amylase, 41 Somogyi units.

Electrocardiogram demonstrated low voltage.

Contrast X-ray studies of the gastrointestinal tract, including barium enema and upper gastrointestinal series, were interpreted as normal.

On September 12, 1966, hepatic scintillography (Figure 3.) disclosed "a large, somewhat round area of decreased activity involving the midpart of the liver and the entire left lobe." Moderate hepatomegaly was also present. Based on these findings, a diagnosis of hepatic amebic abscess was raised.

Emetine and chloroquine therapy were initiated on September 14, 1966. Within 48 hours the white blood count and temperature returned toward normal. More striking was the

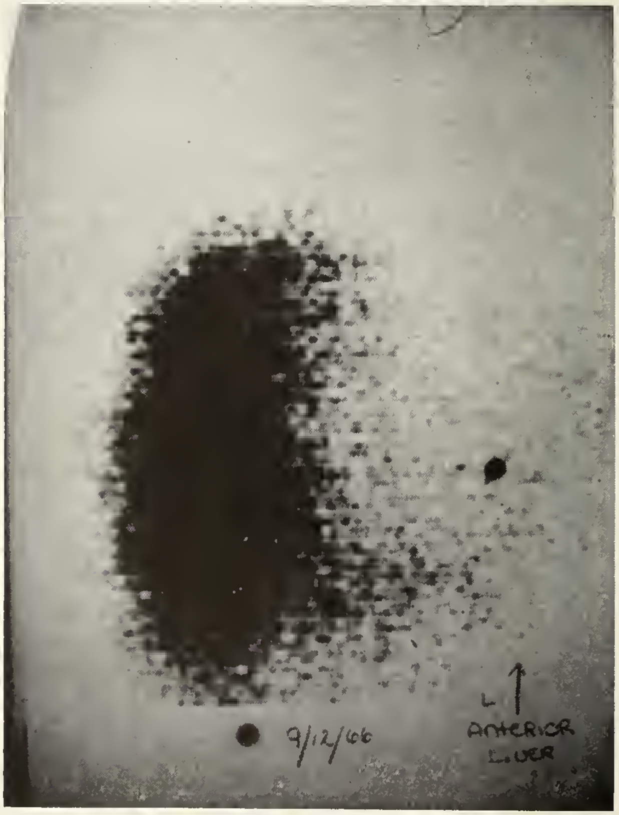

Figure 3

Anterior liver scan in Case II. prior to anti-amebic therapy, illustrating enlarged right hepatic lobe and markedly decreased isotope uptake in left hepatic lobe.

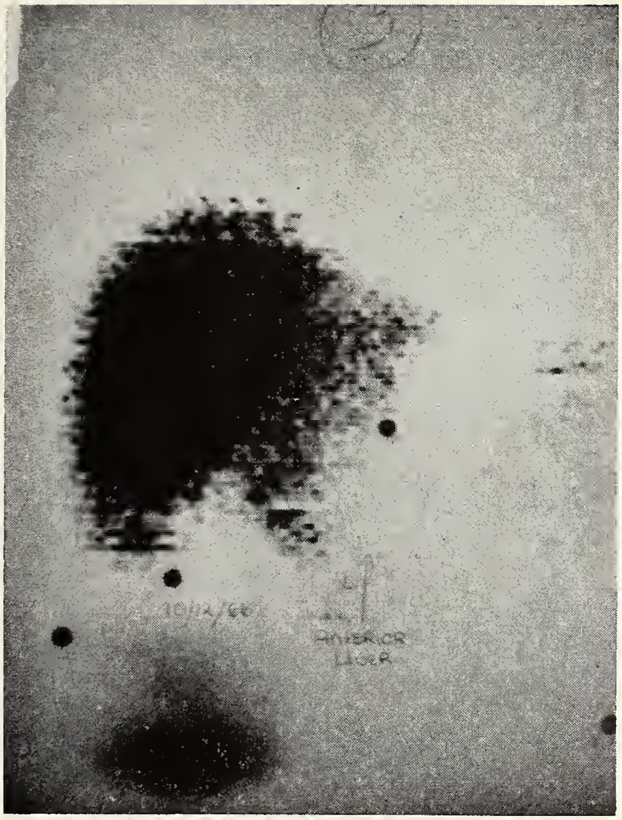

Figure 4

Anterior liver scan in Case II. after eight days of chloroquine and emetine therapy. Note marked diminution in liver size and partial return of isotope uptake in left hepatic lobe.

dramatic improvement in the patient's general condition, morale, and sense of well-being. The entire clinical picture continued to improve. When hepatic scanning was repeated on September 22, 1966, (Figure 4.) it was interpreted as showing "the size of the liver to be nearly normal." The previously noted large area of decreased activity showed also a considerable reduction in size. Bromsulfalein retention, 37 per cent on August 2, 1966, was 5 per cent on September 23, 1966.

Total anti-amebic chemotherapy in the hospital consisted of 455 milligrams of emetine over a seven day period and 7.28 grams of chloroquine over a period of 11 days. Serial electrocardiographic tracings during emetine therapy revealed no evidence of toxicity of the drug to the myocardium.

No amebae were ever demonstrated, though a thorough search was made by examination of stool and drained pus. Hemagglutination testing for extrahepatic amebiasis was positive.

The patient was discharged on September 25, 1966, in good condition, with a non-draining, healing wound, to continue his anti-amebic therapy on an out-patient basis.

COMMENT: This case is of interest because of the difficulties encountered in diagnosis. The location of the abscess in the left hepatic lobe, as well as the absence of corroborative history, contributed to this difficulty. The spontaneous rupture of the abscess with evacuation through the drain site provided the initial incentive for definitive diagnosis. The recently developed indirect hemagglutination test[2] was of real value in confirming the diagnosis in the absence of demonstrable amebic cysts or trophozoites. The excellent response to anti-amebic therapy was again demonstrated.

CASE III: G. H., a 50-year-old white female, was admitted to the Stamford Hospital on August 7, 1967, complaining of upper midline and left-sided abdominal pain, with left shoulder radiation, of four days duration. One month prior to admission the patient, a frequent international traveler and housewife, had traveled to Africa and Italy. During her trip she developed diarrhea which she treated symptomatically, being accustomed to diarrhea during her previous travels. Her diarrhea continued intermittently following her return home. Four days prior to admission she developed fever associated with sweating and the onset of pain in her upper midline and left abdomen with left shoulder radiation. No further pertinent history was noted.

Positive physical findings were limited to a temperature of 38 degrees Centigrade, left upper abdominal tenderness, and a Grade II/VI precordial murmur. No other abnormalities were noted on abdominal or thoracic examinations.

Laboratory findings revealed the following: hemoglobin, 13.0 grams per cent; hematocrit, 39 per cent; white blood count, 17,600 per cubic millimeter with 88 polymorphonuclears, 4 lymphocytes, 4 monocytes, and 4 eosinophiles; sedi-

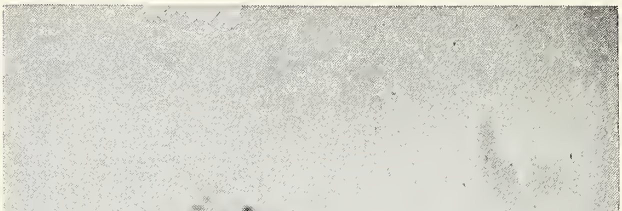

Figure 5

Initial anterior liver scan in Case III. Note marked hepatic enlargement, multiple areas of decreased isotope uptake in both hepatic lobes, with "net pattern" of decreased uptake (See text).

mentation rate, 38 millimeters, corrected; platelets, 373,000 per cubic millimeter; urinalysis, normal; serum sodium, 138 milliequivalents per liter; serum potassium, 3.8 milliequivalents per liter; serum chloride, 99 milliequivalents per liter; serum carbon dioxide content, 27 milliequivalents per liter; blood sugar, 142 milligrams per cent; serum glutamic oxalacetic transaminase, 54 units; serum lactic dehydrogenase, 91 units; serum alkaline phosphatase, 10 King-Armstrong units; serum bilirubin, 0.5 milligrams per cent. Stools were negative for parasites, including amebae. Febrile agglutinins were consistent with anamnestic reaction secondary to recent vaccination.

X-rays of the chest and abdomen were negative. Intravenous pyelogram was normal, and intravenous cholangiography revealed non-visualization of the biliary tree.

On admission it was felt that the patient was suffering from an enteric infection. While diagnostic studies were initiated, bed rest and antimicrobial therapy (ampicillin) were instituted without improvement in the patient's condition. The fever, diarrhea and malaise persisted. Proctoscopy revealed only a tiny sessile polyp.

On August 11, 1967, she was found to have marked hepatic tenderness. Meanwhile, an elevation of serum alkaline phosphatase of 17 King-Armstrong units had occurred. Hepatic scintillography performed on August 11, 1967, (Figure 5.) using radiogold, showed the liver to be enlarged with several areas of markedly diminished isotope uptake. At this time a presumptive diagnosis of multiple amebic hepatic abscesses was made, ampicillin was discontinued, and anti-amebic therapy consisting of chloroquine, two grams daily for two days and 0.5 grams for twenty-one days; emetine, 65 milligrams intramuscularly for seven days; and diiodoquine, 650 milligrams daily for twenty-one days was given.

Clinical improvement was dramatic within twenty-four hours of initiation of specific treatment. Temperature returned to normal within seventy-two hours and remained normal thereafter. Liver tenderness subsided, and the patient's sense of well-being returned.

On August 21, 1967, repeat hepatic scan (Figure 6.) revealed diminution in the size of the intra-hepatic lesions without decrease in liver size. The patient was discharged on August 26, 1967, asymptomatic and with normal physical findings except for mild epidgastric tenderness; liver size was clinically normal. Serum glutamic oxalacetic transaminase was 38 units; serum alkaline phosphatase was 24 King-Armstrong units; serum bilirubin was 0.5 milligrams per cent. Electrocardiogram, monitored throughout emetine therapy, remained normal. At no time were amebae demonstrable, though repeated stool examinations were performed.

Indirect hemagglutination tests and complement fixation tests for amebiasis were positive. On September 19, 1967, serum glutamic oxalacetic transaminase, serum bilirubin, and serum alkaline phosphatase values were normal.

Follow-up liver scan on October 6, 1967, (Figure 7.) revealed complete restitution of liver substance.

COMMENT: This patient presented a clinical picture strongly suggestive of amebic hepatic abscesses with concomitant amebic colitis.

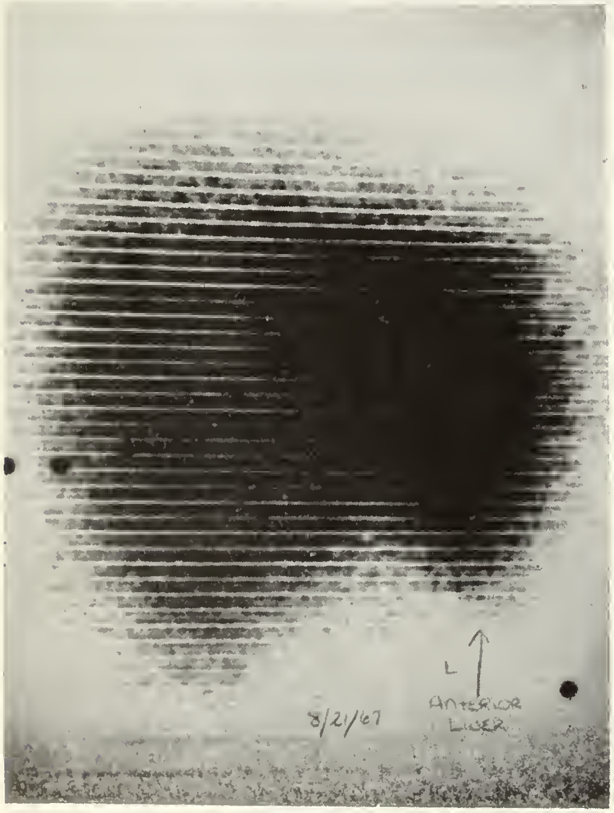

Figure 6

Anterior liver scan in Case III. after ten days of anti-amebic treatment. Note return of uniform isotope uptake, though liver remains enlarged.

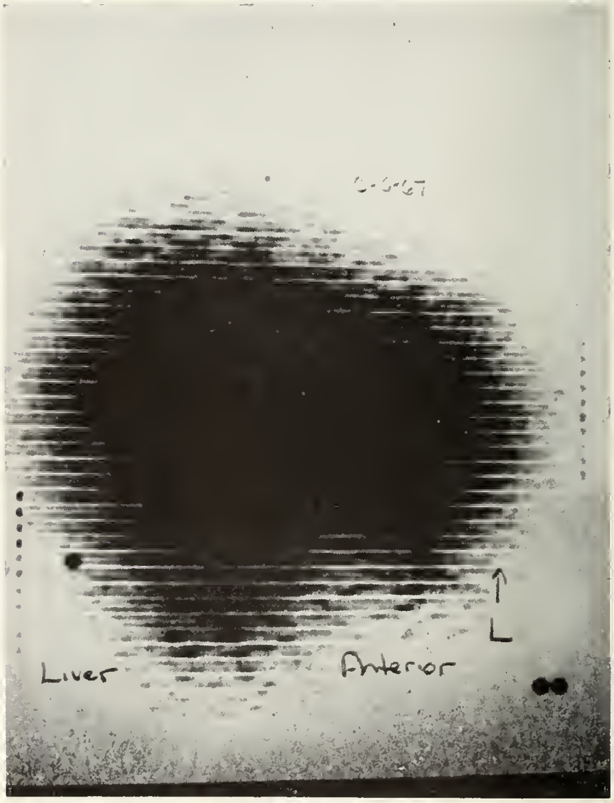

Figure 7

Anterior liver scan in Case III. following completion of therapy, showing return of scan to normal.

The presence of hepatic amebic abscesses in the left lobe of the liver, as seen here, has proven considerably more common than recognized prior to the utilization of hepatic scintillography; multiple abscesses, also present in this case, have also been demonstrated with increasing frequency.

Specific anti-amebic therapy resulted in complete clinical recovery, verified by liver scan, emphasizing once again that neither aspiration nor other forms of surgical treatment are essential in the management of the uncomplicated hepatic amebic abscess.

Confirmation of the diagnosis of extra-intestinal amebic disease was possible by serodiagnostic methods.

DISCUSSION: The criteria applicable to a diagnosis of hepatic amebiasis have undergone considerable evolution during the past decade as a result of the development of specific serodiagnostic and radioisotope techniques. We feel that the syndrome of hepatic amebiasis can be defined as consisting of 1) an enlarged, tender liver, usually associated with fever, 2) suggestive hematologic findings, 3) suggestive radiographic and hepatic scintillographic findings, 4) specific serodiagnostic tests, and 5) response to specific anti-amebic therapy.

Tender hepatic enlargement accompanied by fever is present in the great majority of cases and is the most consistent physical finding.[3] A history of amebiasis and the presence of stool organisms, when present, are of great value to the diagnosis; however, the majority of patients deny diarrhea. Turill and Burnham[4] were able to identify trophozoites in only 26 per cent of their recent series. The value of aspiration of pus from the amebic hepatic abscess as a diagnostic and therapeutic maneuver has been eclipsed 1) by the rapid and complete resolution of amebic abscess in response to anti-amebic chemotherapy, 2) by more reliable serodiagnostic tests, and 3) by the introduction of precise evaluation of the response to therapy by scintillography.

Despite the striking clinical picture of a severely ill, febrile patient with tender hepatomegaly, the results of hematologic and liver function studies may show very little alteration. Leukocytosis and elevated sedimentation rate are usually noted; anemia is not uncommon, especially in long-standing or severe disease. The most commonly disturbed liver function tests are alkaline phosphatase, bromsulfalein excretion, and glutamic oxalacetic transaminase determinations. Jaundice is less commonly noted, but where more than moderate rises in serum bilirubin are present, the associated hepatic abscess is usually large.

Roentgenologic changes most often seen in complicated cases of hepatic amebic abscess are essentially those suggesting subphrenic infection and include diaphragmatic elevation and/or immobility, or pleural effusion.

Although contrast studies such as pneumo-peritoneum, to demonstrate hepatophrenic fixation, and contrast injections of abscess cavities have been utilized in the past, these techniques are now rarely required for diagnostic or therapeutic purposes.

Hepatic scintillography, utilizing isotopes of either gold or rose bengal, has become a vital adjunct to the diagnosis and therapy of this disease. From the standpoint of diagnosis the hepatice scan reveals characteristics changes consisting of 1) diffuse liver enlargement, 2) diffuse, mild diminution of isotope activity as compared to the normal and 3) a focal filling defect in the hepatic mass with a "net pattern." This latter aspect of the scan has been differentiated by Tandon et al.[5] from the "hole-like" defect in scans of livers containing malignant tumors. The net pattern is thought to result from the fact that the abscess is almost always surrounded by functional parenchyma and that trabeculae of functioning cells traverse the abscess locus. The relation of the scan to therapy involves the quantitative evaluation of the size of the liver and of the abscess cavity in response to chemotherapeutic agents. Utilizing serial scans it has proven possible to demonstrate accurately the total disappearance of abscesses without resort to surgical intervention; further, it has become evident that adequate drug therapy must be judged in reference to such demonstration. Scintillography has also shown that multiple abscesses, left lobar abscesses, and abscesses in cases formerly considered "amebic hepatitis" are considerably more common than was heretofore appreciated.

Since it is known that Endamoeba histolytica can be either a non-invasive commensal organism or a pathogen, it is obvious that the recovery of trophozoites or cysts of Endamoeba histolytica in the stool may or may not in itself connote clinical disease. Serodiagnostic techniques for the diagnosis of amebiasis were first employed by Izar,[6] Scalas,[7] and Craig;[8] after several years, however, the method was abandoned because of high rates of negative results in the presence of known invasive amebiasis. This failure was attributable to technical difficulties in preparation of standardized antigen. Recent advances in antigen preparation have again established the usefulness of such tests.[9] Serologic study, in addition to providing a more objective diagnostic approach, has the advantage of implying tissue invasiveness of the ameba or its products. In addition to the modified complement fixation test for amebiasis, the indirect hemagglutination test described by Lewis and Kessel[10] in 1961 has provided another reliable serodiagnostic means for the detection of circulating antibodies for Endamoeba histolytica. To date these tests are available only in specialized laboratories as confirmatory evidence in highly suspected and thoroughly investigated cases.[2] The complement fixation and indirect hemagglutination tests are highly positive in essentially all cases of hepatic amebiasis. Except in the rare instances of failure to produce immunologic response, negative indirect hemagglutination or complement fixation tests virtually exclude the presence of hepatic involvement. Since either test may remain positive for prolonged periods following successful therapy, their usefulness in evaluating therapy response is obviously limited.

Today the drug of choice for the treatment of hepatic amebiasis is chloroquine, with or without concomitant emetine. The accepted dose of chloroquine varies from 0.5 gram daily for 21 days, to the same total dosage over a two month period; the dose of emetine is 60 milligrams daily for seven days. Therapy cannot be considered complete until the liver scan returns to normal. In order to prevent recurrence of extra-intestinal disease it is of utmost importance to institute therapy directed at the eradication of possible intestinal amebiasis. For this purpose repeated administration of oxyquinolines, arsenicals, and/or amebicidic antibiotics should be employed until several negative stool examinations for trophozoites and cysts are obtained.

Recent editorial comment to the contrary,[11] it is apparent that the indications for surgical maneuvers, including aspiration of abscess, in the management of hepatic amebic disease are becoming progressively narrower. Whereas abscess aspiration provides confirmatory diagnostic evidence, this is not a necessity in the usual case, especially since the pus obtained may not be typical and since amebic organisms are commonly absent from the abscess contents. Nor is aspiration a therapeutic necessity since drug therapy usually accomplishes cure and since cure can now be measured by serial hepatic scintoscans. Indications for surgical intervention by closed or open procedures at this time would seem to include the following circumstances: 1) the unusual case which fails to respond to drug therapy, 2) the case with secondary pyogenic infection within the abscess cavity, and 3) cases of ruptured abscesses with involvement of other organs or abdomino-thoracic spaces.

SUMMARY: Three cases of hepatic amebiasis treated recently at the Stamford Hospital have been presented with a view to emphasizing current concepts of diagnosis and management of this disease.

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Scintillation Scanning in a Community Hospital A Review: Part IV

Chester J. Kay, M.D.

Liver Scanning

Liver scanning accounts for a significant percentage of the work done in nuclear medicine because of the abundance of satisfactory isotopes to study the organ and the inability to adequately evaluate its morphology clinically and radiographically.

The liver is composed of polygonal and reticuloendothelial (Kupffer) cells. I-131 labeled Rose Bengal is removed from the bloodstream by the polygonal cells and is excreted thru the biliary tree into the small bowel. In a normal patient the isotope should be demonstrable in small bowel at one hour (Figure 1). There may be some delay in patients who are taking Thorazine or similar drugs. If the material is not excreted into the small bowel, at one hour, and there is not major damage to the liver as determined by the method of Nordyke[1] prior to the scan, the diagnosis of extrahepatic biliary obstruction may be made. This test has been quite accurate in our hands[2] and the hands of others[3]. We do not use Rose Bengal I-131 for routine scans because of its rapid excretion and the occasional superimposition of the gall bladder and small bowel over the liver which may obscure pathology.

Radioactively labeled colloidal particles ranging from 0.1 micron to 1 micron are phagocytized by the Kupffer cells. Gold-198 falls into this group and is probably the most widely used liver scanning material in this country. Technetium 99m labeled sulfur colloid,[4] microaggregated I-131 labeled albumin[5], and indium 113m colloid[6] are similar agents used for liver scanning. Technetium 99m sulfur colloid and indium 113m are prepared prior to each injection from a generator. They are particularly valuable if one uses a scintillation camera because of the high count rate obtained.

Any one of the agents may be used for the determination of liver size and configuration (Figure 2). These may vary considerably as Mc Afee has diagramatically depicted[5]. Areas of non-function ap-

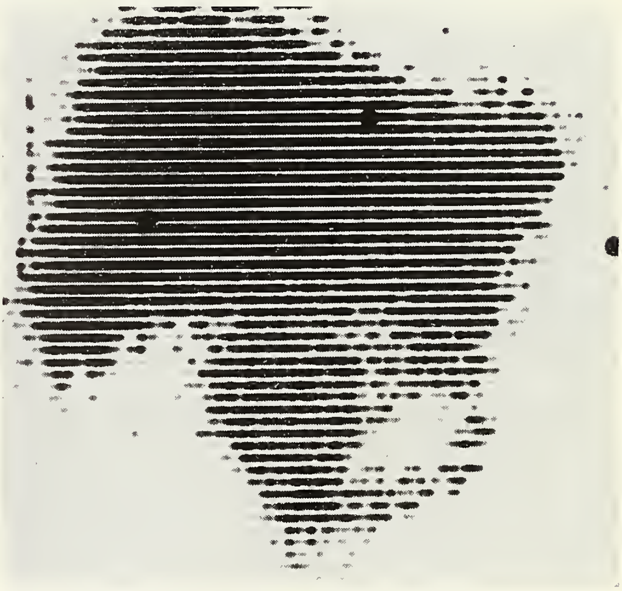

Figure 1

Normal anterior liver scan performed with I_{131} labelled Rose Bengal. Note the activity in small bowel. Compare with figure 2 where scan was performed after radiogold injection and no small bowel activity is present.

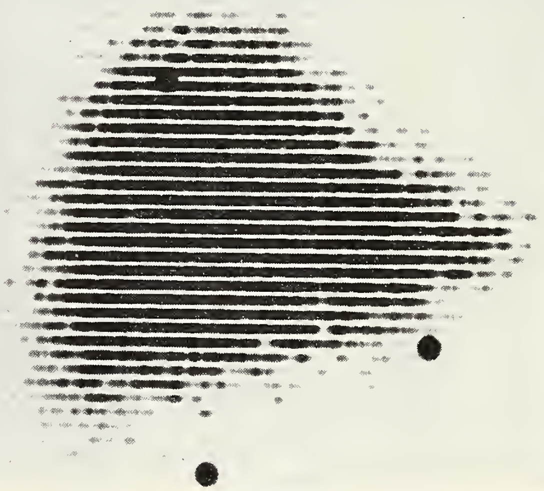

Figure 2

Normal liver scan performed with colloidal gold-198.

DR. CHESTER J. KAY, Associate Attending Radiologist Park City Hospital, Bridgeport, Connecticut; Clinical Instructor in Radiology, Albert Einstein College of Medicine.

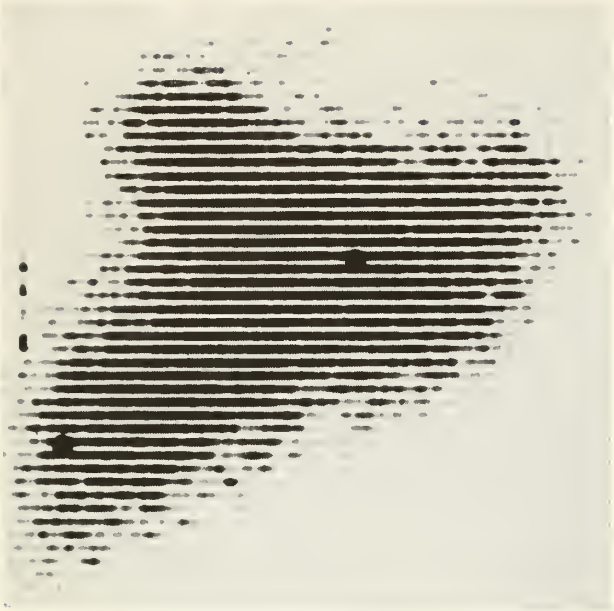

Figure 3

Metastatic deposit in the right lobe of the liver. Note the large filling defect.

pear as filling defects on the scan (Figure 3). There are several factors which limit the ability of the scan to delineate these, and therefore decrease the accuracy of the test. The scan is commonly done with a collimator focused at a point in the organ. A small lesion above or below this point may be partially obscured. Since a single view may take 10 or 15 minutes respiratory motion may blur or hide a small peripherally located lesion. Under optimal conditions, the scan can depict lesions 1 inch or larger. However, in one autopsy series, 30% of metastatic deposits were 2 cm. or smaller. This compares with the approximate 75 to 80% accuracy of scans in demonstrating these lesions. Studies comparing the accuracy of liver function tests[7], scanning, and surgery have shown the scan to be superior to chemical tests and about as accurate as surgery[8] since the surgeon cannot see deep seated lesions or lesions near the dome of the liver. The false positive rate is about 15%.

Many entities can produce cold areas in addition to metastases. Some of these are primary hepatic tumors, both benign and malignant, abscesses, cysts, infarcts, hematomas and fibrotic nodules. Highly vascular tumors such as hemangiomas and some sarcomas may appear cold on a radiogold scan and be "hot" or fill in on a scan using I-131 labeled human serum albumin. Inflammatory processes in the gall bladder can produce a defect in the adjacent liver. The scan may also be used to help pinpoint a good site to biopsy the liver. It has been helpful in screening patients with jaundice of undetermined etiology and in differentiating whether a palpable abdominal mass represents functioning liver. The combination liver and lung scan is sometimes useful in demonstrating a subphrenic abscess.

Normally there is a small amount of pickup in the spleen when one uses a colloid to scan the liver. In cirrhosis and other diseases diffusely replacing liver tissue such as some granulomatous processes, myelofibrosis and occasionally lymphomas, the radiocolloid is diverted from the liver to other areas of reticuloendothelial concentration. Patchy hepatic concentration and pickup in the spleen and bone marrow characterize these processes (Figure 4). At times, areas of fibrosis may be so large as to cause confusion with hepatomas or metastatic disease.

Current improvements include rapid scanning with cameras, the development of scanning tomography, and the use of positron emitting isotopes which permit focusing in depth.

Spleen Scanning

The demonstration of splenic morphology is usually unsatisfactory on coventional abdominal films, and may be incomplete with such special procedures as arteriography or retroperitoneal air insufflation.

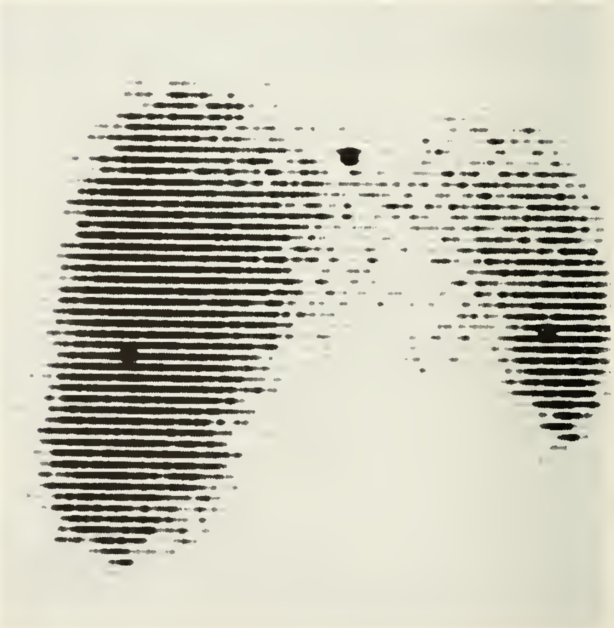

Figure 4

Portal cirrhosis, radiogold scan. Note the enlarged liver extending beneath the costal margins (large black dots) with pickup in the spleen.

The current methods of spleen scanning fall into two categories; a) sequestration of tagged red blood cells after they have been altered thermally[9], chemically[10], or immunologically[11]; and b) the nonspecific accumulation of radioactive colloidal material by the reticuloendothelial cells after intravenous injection[12].

Examples of the first group are chromium-51 tagged red cells injured by heat or sensitized with anti-D serum and red cells damaged and tagged by mercury-197 labeled mercurihydroxypropane. Into the latter category falls the injection of technetium 99m labeled sulfur colloid, I-131 labeled colloidal albumin, indium 113m colloid and larger doses of gold-198 than customarity used for a liver scan. The patient is conventionally scanned in the posterior and left lateral position with more views being obtained as required. The normal spleen appears as an oval, circular, or comma shaped structure.

The scan is valuable in; a) the differential diagnosis of left upper quadrant masses; b) the diagnosis of splenomegaly; c) the identification of accessory splenic tissue; d) the diagnosis of granulomas and mass lesions in the spleen (which appear as "cold" areas); e) the detection of abscence of splenic tissue and; f) the identification of vascular lesions such as infarcts, and traumatic rupture.

Bone Scanning

Radiologic detection of metastatic lesions in bone requires that 30 to 50% of the mineral content be lost. Correlation of radiographic and autopsy specimens shows the inability of roentgenographic studies to detect 50% of bony metastases. The clinical need for earlier and more accurate detection is obvious. Since the early use of gallium-72 in detecting areas of osteogenesis[13], interest in the application of radioisotopes in cancer detection increased. Of the radioisotopes that have been tried, strontium-85 is the most widely used. Others being used or investigated include strontium-87m, fluorine-18, calcium-47 and gallium-68. Fluorine-18 appears most satisfactory[14] but its short half-life has prevented broad commercial application. The metabolism of strontium is similar to that of calcium. Bone biopsy or autopsy specimens from 34 cancer patients[15] showed that the strontium was deposited in proliferating new bone in and around the lesion. Thus the scan seems to depict relatively early activity of the process whereas the roentgenogram shows the later net result of the destructive and reparative processes. If the disease process is not active, or if it is small, it may not be seen on the scan.

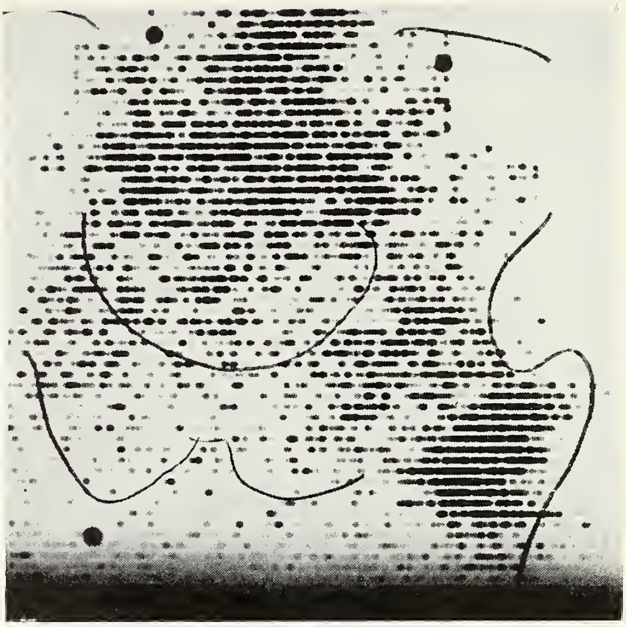

Figure 5

Metastatic adenocarcinoma to the left femur and lumbar spine. Activity may normally be somewhat increased over the sacro-iliac area. The scan was performed with Sr^{85} five days after injection.

50 to 100 microcuries of strontium-85 is injected intravenously. The scan may be performed 2 to 7 days later. The bowel must be cleansed by enemas since part of the isotope is excreted into it. The low count rates usually obtained require slow scan speeds. Radiostrontium is deposited in all bones where osteoblastic activity is present. It is normally present in increased quantity around the epiphyses of children. Articular cortices and joints may show increased activity in the adult. Primary or metastatic tumors appear as one or more hot (black) areas in comparison to normal surrounding bone (Figure 5). In the differential diagnosis are benign lesions which may also produce a positive scan. These include fractures, osteomyelitis, Paget's Disease and some benign tumors.

Summary

This series of papers has summarily presented some of the highlights of this rapidly growing and dynamic area of medicine. Many new radionuclides and clinical applications are being tested which are beyond the scope of this review. It is hoped that with further improvements in instrumentation, scintillation scanning will continue to grow and contribute to patient care.

Acknowledgement: To Mrs. Mary Stephenson for her invaluable help. To JoAnn Chill and Eleanor Machunk for assistance with the manuscripts.

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"Tube Ostomy" To Avoid Nasal Intubation

"I hate to think of myself lying in a hospital bed for a period of time [after colonic or rectal surgery] with a tube down my nose. So I do an awful lot of 'tube ostomies.' I put in just a couple of purse strings [sutures]; and then . . . I make sure that I get the tube through a little piece of omentum some place or through some fatty mesentery or something some place. I also make the tract as long as possible; and I don't sew the stomach against the peritoneum. There's not going to be any leakage if there's a little omentum there. But I make the tract a long one, and it won't stay open. The length of the tract, I think, is tremendously important."—William C. Beck, M.D., Philadelphia. Extracted from *Audio-Digest Surgery*, Vol. 15, No. 22, in the Audio-Digest Foundation's subscription series of tape-recorded programs.

A Methodology for Studying the Emergency Care of the Trauma Patient: Results of the Yale Trauma Study

Kristaps J. Keggi, M.D., Samuel B. Webb, Jr., MPH, and Ernest J. Broadbent, B.A.

Intoduction and Definition of the Problem

At present, accidents are the leading cause of death between the ages of 1 and 44 years[1] and it is recognized that multiple factors contribute to such trauma. Only fragmentary information is available about the communication, transportation and medical care components of existing emergency medical care systems designed to cope with accidental injury but it is obvious that there is much room for improvement in these areas.[3-4] The record of lives saved in Vietnam contributes to this feeling and has stimulated a re-evaluation of civilian systems of emergency medical care.[5] Many hopitals, medical schools and physicians are exploring the role, function, organization, staffing and adequacy of emergency departments to meet the needs and demands of the patient populations they serve.[6] Available evidence indicates that the following questions need further exploration:

1. Is basic emergency care receiving adequate time in medical school curricula?
2. Do interns and residents have the opportunity to learn the principles of managing acute trauma?
3. Are the existing specialty groups sufficient for the total management of a patient with multiple trauma?
4. Is our legal system aware of and organized to respond to current problems in emergency medical care?
5. Are emergency crews receiving proper training in emergency first aid techniques?
6. Should technicians with a high school education be trained and given a career incentive in the field of emergency care and transportation?
7. Should the need for better coordination of total emergency care systems, adjoining several communities into one broad catchment area be investigated?

In the past, the tendency has been to approach the problem by concentration on relatively well-defined areas of the total field[7] which has led to a "cellular view" of trauma. An interdisciplinary effort seems a minimum prerequisite if facts are to be learned and, as a first step, administrative and medical input have been welded to produce a joint effort between the Departments of Surgery and Epidemiology and Public Health in the Yale School of Medicine, the Department of Administrative Sciences in the University, and the Yale-New Haven Hospital and titled the Yale Trauma Study. This exploratory project is designed, through the development of logical methodology, to investigate the set of events which occur after an accident takes place. It is hoped that an analysis of the data will enable the diverse contributing factors of accidents and trauma to be explored and gaps in present knowledge identified.

Methodology

The study is designed to explore the relationships of accidents and trauma to the medical care, communications and transportation components of an emergency medical care system. Basic to this methodolgy is the concept of a trauma registry defined as a central agency for the collection of clinical, pathological, and epidemiological, data for systematic study. Other important definitions are: *Trauma*—"An injury or wound violently produced."[8] *Accident*—"An event that takes place without one's foresight or expectation usually resulting in a wound or injury."[9] The population at risk in the present study is the New Haven Standard Metropolitan Statistical Area (SMSA). In addition to

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the City of New Haven, this includes the Towns of West Haven, East Haven, North Haven, and Hamden, Connecticut. The following functional activities have been designated:

A. *Definition of the problem through the creation of a Trauma Registry*

B. *The Development of an Index of Injury Severity*

C. *Analysis of the Effectiveness of Television in the Management of the Trauma Patient*

D. *A System Analysis of Emergency Medical Care Sub-systems and their Relationships*
   1. Communication sub-system
   2. Transportation sub-system
   3. Medical care sub-system

E. *Development of Sub-system Simulation Models*
   1. Emergency Room models
   2. Communication models
   3. Transportation models
   4. Cost models

F. *Validation of Models*

G. *Analysis of Cost, Effectiveness of Alternative System Relationships*

H. *Identification and Exploration of Contributory Factors Producing Trauma and Injury-producing Accidents*

To date the folloing activities have been initiated:

A. Definition of the problem through the use of a Trauma Registry

B. Development of an index of injury severity

C. Systems analysis of the New Haven, Connecticut emergency medical care sub-system and their relationships

D. Analysis of the Effectiveness of Television in the management of the trauma patient

E. Development of sub-system simulation models

This paper will report on the results of data collected through the use of a Trauma Registry in a population composed of 1,123 visits to the Yale-New Haven Emergency Service between November 16 and December 15, 1967. Only patients diagnosed as victims of trauma were included in the registry and repeat visits by one person were recorded separately if, indeed, each visit had trauma implications. Data were obtained for each patient through a predesigned trauma registry coding sheet.

Five registered nurses stationed in the emergency room provided continuous coverage and enabled data to be collected twenty-four hours per day for four weeks. In addition, various physicians gathered appropriate data if the patient was admitted to the hospital. The five nurses, in accord with pre-established instructions and with the consultation of physicians, determined whether or not the condition of the patient was traumatic. Transients and patients dead on arrival made up a small number of cases (0.2%) in which little or no information was available.

Findings

A. Trauma Population, the population at Risk and the general Population using the Yale-New Haven Emergency Room

In order to plan effective emergency medical services, it is felt that one must know the social and demographic characteristics of the population demanding such services. Such information can enable a community to make the important determination as to how emergency services for accidents and trauma can be focused toward the total population at risk and toward specific segments of the population. For this purpose, data from our Trauma Registry is compared with the results of a 1966 study of the Yale-New Haven Emergency Room[10] and with special census data collected in a 1967 survey of the New Haven SMSA. For comparative analysis in the following data, the chi-square test of statistical association was employed with a probability level of 0.5 accepted as significant.

Age

The Trauma Population and the general emergency room population sample (includes both urgent and non-urgent cases) show no significant differences in terms of age. Both populations are composed of significantly more children and young adults that would be expected from the population at risk.

Sex

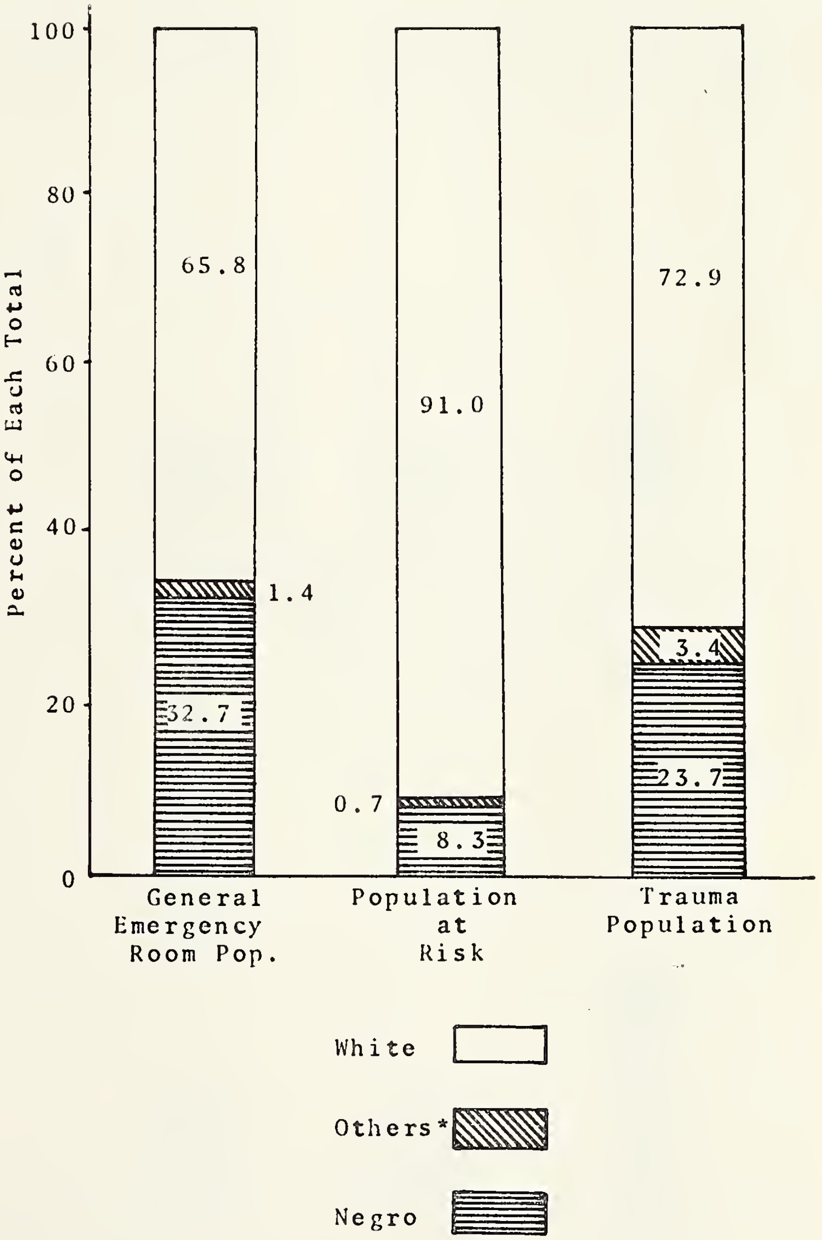
The Trauma Population is composed of significantly more males (65%) compared to both the population at risk (49%) and the general emergency room population (58%).

Non-white Group Status

Figure 1 illustrates that both the general emergency room population and the trauma population show significantly more non-whites than the population at risk. However, there are significantly fewer non-whites in the trauma population (23%) than the 34% in the general emergency room population.

Employment Status and Income

Figure 2 shows the unemployment rate of the trauma population to be 6.1% compared to 4.4% for the population of risk. Statistically this is not significant. However, both are significantly lower than the 21.7% unemployment rate reported in the general emergency room population. In terms of income, Figure 2 shows that there is no significant difference in the percentage distribution of individuals in the income category below $5,000 and in the $10,000 or over category between the trauma population and the population at risk. When compared with the general emergency room population, both the trauma population and the population at risk are composed of significantly fewer individuals in the below $5,000 category and significantly more individuals in the $10,000 and over income category. In the category $5,000 to $10,000 the general emergency room sample and the trauma population are essentially the same while both are substantialy below the population at risk.



* Includes those recorded as Puerto Rican and Oriental

Figure 1
Percentage Distribution by Color

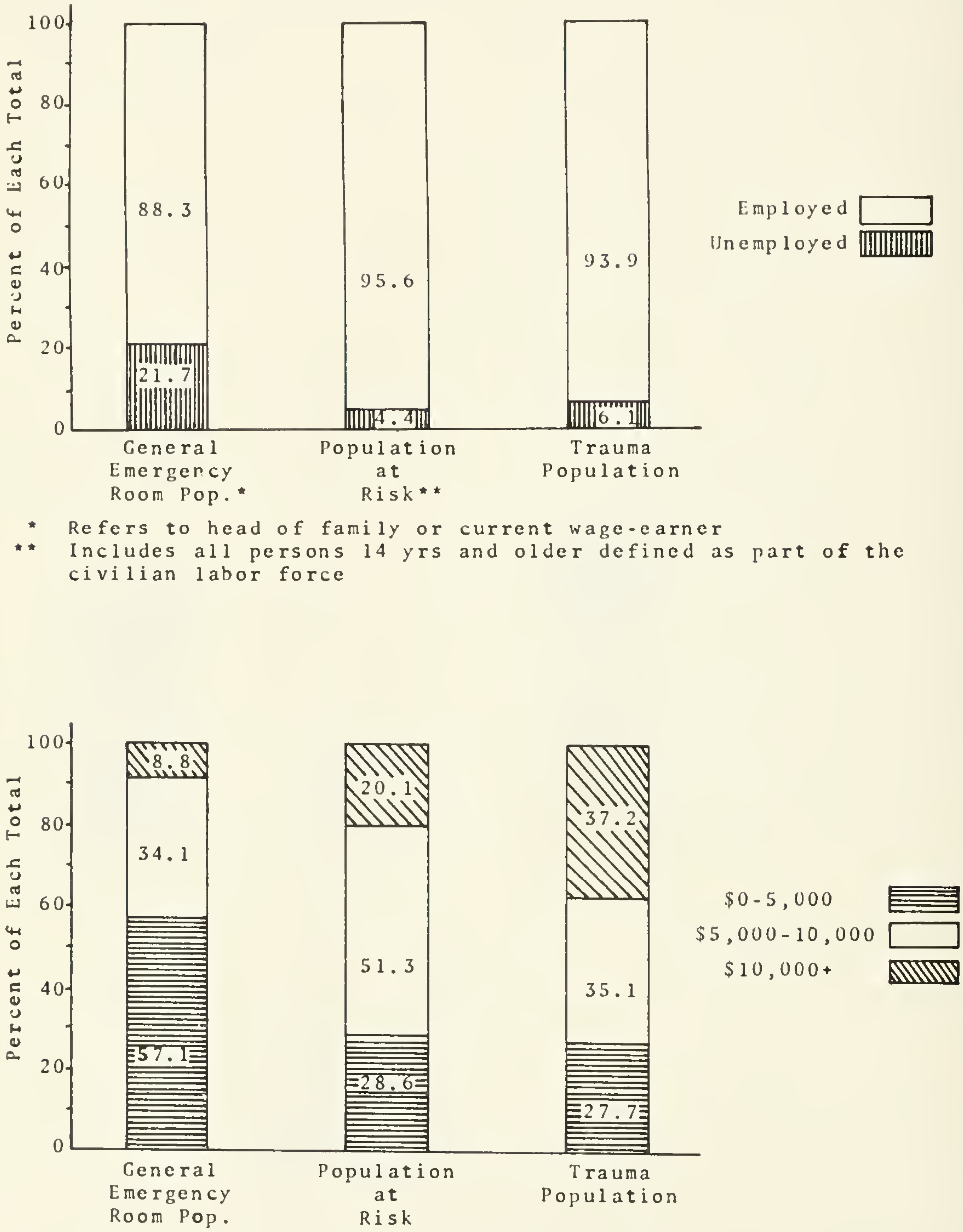
Marital Status

Both the trauma population and the general emergency room sample are composed of significantly higher proportions of individuals in the separated and/or divorced, single, and widowed categories than the population at risk. However, significantly fewer married individuals are in the trauma population (37.5%) than the general emergency room population (51.3%).

Education

In spite of the fact that there are more individuals in higher income groups and significantly less unemployment in the Trauma Population and the population at risk compared to the general emergency room population, there is no significant difference between the three populations in terms of level of education.

An analysis of trauma in relation to day, time, first aid treatment instituted at the scene, medical



* Refers to head of family or current wage-earner
** Includes all persons 14 yrs and older defined as part of the civilian labor force

Figure 2

Percentage Distribution by Employment Status
Percentage Distribution by Family Income

services provided and the location of accidents involving the trauma population through census tracts established by the United States Census Bureau for the New Haven SMSA.

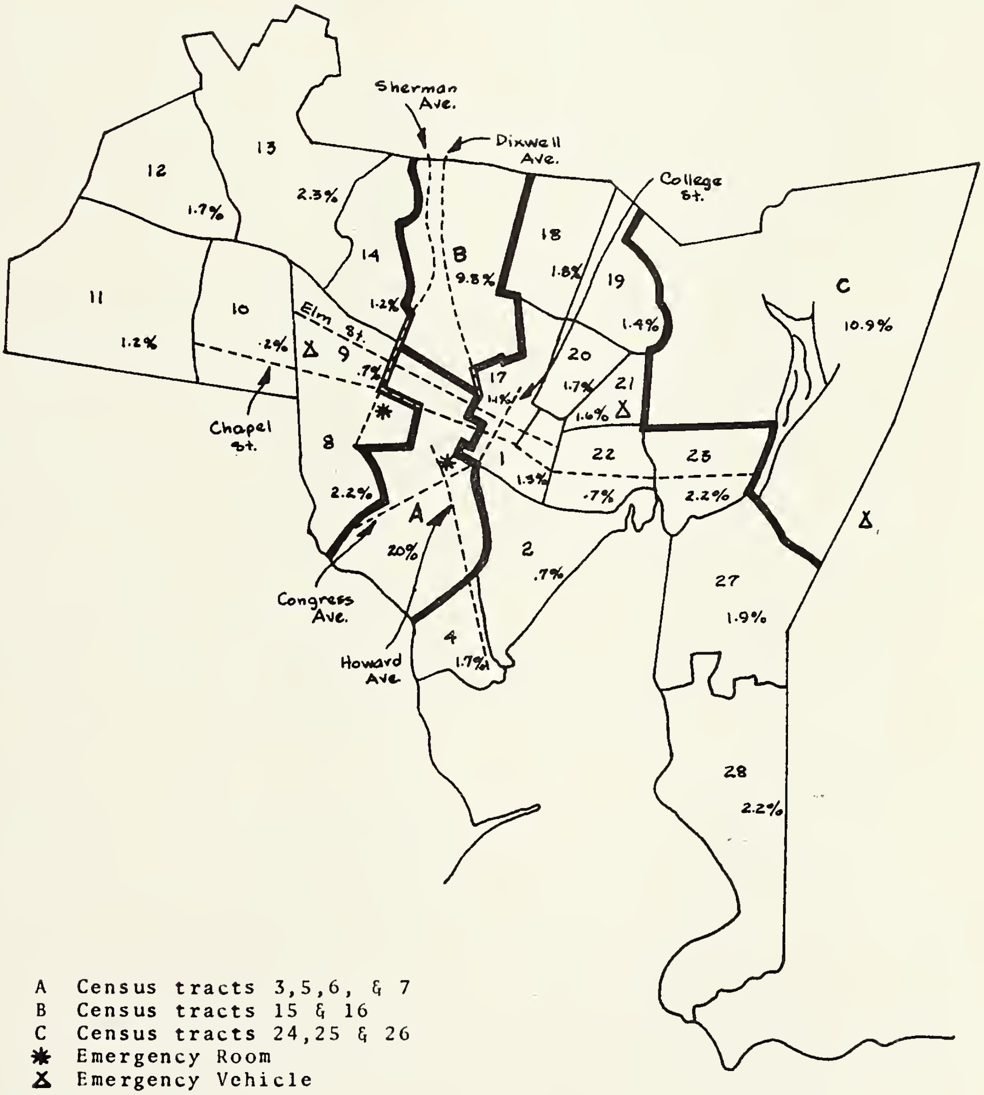
Figure 3 shows the location of all Trauma cases in New Haven, Connecticut in addition to the location of institutional and non-institutional emergency services. New Haven accounted for 64.2% of all registry cases in the study. Interestingly, over 20% of all cases were located in relatively close proximity to the Yale-New Haven Hospital (Census tracts 3, 5, 6 and 7). The remainder were fairly evenly distributed throughout the New Haven SMSA, except for two fairly circumscribed areas. Census tracts 24, 25 and 26 accounted for 10.9% of the cases and Census tracts 15 and 16 accounted for 9.8%.

Day of Occurrence

As might be anticipated, Friday, Saturday and Sunday prove to be the peak days for trauma incidence comprising about 48% of the registry population, the remaining being evenly distributed among the rest of the days of the week.

Time of Occurrence

Approximately 75% of all trauma patients presenting themselves at the emergency room do so between the hours of 5 p.m. and 4 a.m. Within this time period, almost 40% arrive between 10 p.m. and 3 a.m. Interestingly, only 16% of the trauma



Total Percent of Trauma Cases in the city of New Haven: 64.2%

Figure 3
Accident Locations by Census Tracts New Haven, Connecticut

patients arrive during the so called working day, (8 a.m. to 5 p.m.).

Treatment at the Scene

Analysis of the trauma registry indicates that paramedical personnel arriving at the scene of an accident performed the following services; splinting of possible fractures in 50% of the cases, administration of oxygen and simple medications in 24% of the cases; dressing of wounds in 19% of the cases. There was no need for first aid in 7% of the cases.

Classification of Primary Injury

Nearly 35% of all the patients studied suffered from lacerations and open wounds. Superficial injuries (abrasions, blisters, or contusions) accounted for nearly 27% of the trauma studied. Fractures and dislocations accounted for 12% of the injured; sprains or strains of joints and/or adjacent muscles accounted for an additional 11%. The remaining 15% of the cases suffered from burns, foreign bodies entering through a body orifice, adverse effects of chemical substances, hyperventilation syndrome, acute brain syndrome associated with alcoholism and injury to the spinal cord.

Medical Services Required

Over 43% of all trauma patients required only emergency room attention. Emergency Room care with ambulatory clinic follow up accounted for 35%, while 13% were directed to their private physician after emergency room treatment. Seven per cent were either admitted directly to the hospital after emergency room treatment or by-passed the emergency room and were admitted to the hospital immediately. The remaining 2% were dead on arrival or expired prior to disposition.

Method of Transportation

Private cars are used the greatest percentage of the time (65%) while ambulances are second, (18%) in terms of utilization by trauma patients. Public transportation and ambulatory patients account for the remaining 17% of the patients.

Analysis of Trauma in Relation to In-hospital Services

Approximately 7% (86) of the 1,123 patients in the trauma registry were hospitalized for diagnosis and/or treatment. Of these patients 43% were admitted to Orthopedic Surgery; 15.3% to Neurosurgery; 10% to General Surgery; 5.9% to Thoracic Surgery; while 15.3% were distributed randomly between the medical, pediatric and ear, nose and throat services. Death as a result of trauma occurred in four cases, accounting for only .35% of the total sample.

Of the 86 hospitalized patients, 6 (7%) were in need of special nursing care on the general floors while in the hospital; 11 (13%) were confined to either the recovery room or the intensive care unit for an average of 3.8 days. The average length of stay for all trauma patients hospitalized was 11.4 days as compared to 8.2 days for all Yale-New Haven Hospital admissions. Over 70% of the patients hospitalized required from one to three blood transfusions, while an additional 16% required from six to eight transfusions.

Of the 86 patients admitted 54 required some type of surgical operation. Of these 59.5% required an orthopedic procedure; 23.7% underwent either general or thoracic surgery; and 16.8% required neurosurgery.

Analysis of Trauma in Relation to Transportation Accidents

Approximately 16% (174) of all trauma patients were involved in some type of transportation accident. Of these, approximately 85% involved automobiles. Interestingly, of the 174 transportation accidents, 53 or over 30% involved an infraction of the law.

Analysis of Trauma in Relation to Safety Devices

Our data indicates that safety devices (industrial devices such as protective glasses and steel shoes in addition to automobile seat belts etc.) which could have prevented or lessened injuries are not being utilized as much as is desirable to prevent or lessen accidental trauma. In the 426 cases where a safety device was provided and would have prevented or lessened the trauma incurred, they were in use only 4.3% of the time. A further analysis shows that in 79% of the transportation accidents the wearing of seat belts could have reduced and/or lessened the resultant injury. Of this 79%, only 20% made use of this important safety device.

Discussion

A comparison of the social and demographic characteristics of the trauma population with the population at risk and the general emergency room population illustrates the fact that any emergency medical system must be designed and organized to serve the total population of a community. Our figures seem to indicate that the higher income groups may use a private physician for their general medical care but go directly to the hospital in the case of an accident or injury. The present system for emergency care in the New Haven SMSA is organized quite well to respond to emergencies. Available transportation and institutional facilities are well located in terms of the existing geographic distribution of trauma. (See Figure 3) However, the collected data raises questions as to what the nature of the response should be. Approximately 91% of all trauma patients require out-patient care for their injuries, and about 80% of the patients were able to reach the hospital in a car, bus, taxi, or by walking. While over 20% of the cases arrived by ambulance or with police assistance, 90% of these did not require hospitalization. In view of these facts, it is questioned whether the present system of maximum medical response to all individuals calling for assistance is economically or medically justified. On the basis of the results of this study it is felt that changes should be made in the existing emergency medical care system in the New Haven SMSA and we would advocate a flexible, multiple response system.

One alternative would call for a mobile triage officer to respond to the scene of an accident for the purpose of evaluating a patient's condition in addition to rendering necessary first aid. Such an individual would decide what (if any) transportation was necessary. Instead of automatically summoning an ambulance, a decision might be made to call a taxicab (medicab), use a police, fire department or commercial station wagon or, indeed, send a special fully-equipped mobile operating room or coronary care unit to render the most appropriate level of medical care at the scene or in transit. Variations of this concept are in use today in West Germany,[11] Ireland[12] and in parts of the United States.[13]

Another alternative would be the establishment of several emergency first aid stations, either as satellites of the local hospitals or under the auspices of the county medical society. These would be staffed by a nurse and/or emergency medical technician under a physician's direction. Such a system would provide citizens with readily available emergency care and make appropriate use of available professional manpower. It would also provide more appropriate utilization of highly specialized, expensive hospital facilities. A system that would direct patients that do not need hospitalization to community physicians should also be explored. A variation of the emergency referral system of the New Haven Medical Association could be used for this type of patient disposition whereby available and interested physicians would absorb a large part of minor trauma. Such a system would be possible only with the cooperation and enthusiasm of community physicians, who should be responsible for planning and implementing such an endeavor.

If one or a combination of these alternatives were implemented, it is felt that the result would be a more rational system of emergency medical care—rational in the sense that the patient would receive the type of emergency transportation and care appropriate to his medical condition in an economical and efficient manner. At present, only maximum response is available, in terms of transportation and medical care, despite the fact that nearly 70% of the trauma patients arrived at the emergency room by walking or driving their own car and over 90% of these patients required only out-patient, ambulatory care of the type available in a private physician's office. Ultimately it is hoped that a system can be designed for New Haven which would allow the evaluation of a trauma victim through a staged process, including first aid stations, the offices of private physicians, trauma centers and finally, when necessary, rehabilitation units.

Of late, there has been much discussion about the feasibility of trauma units in general hospitals.[14] We believe that our data on the inpatient services required for patients with trauma implications will provide a necessary input into the design, function, and organization of such a unit. Our data regarding the day of the week and time of occurrence indicates that there can be no rigid pattern in terms of staffing an institutional facility designed to care for the trauma patient. However, certainly the specialties of orthopedic surgery, general surgery, neurosurgery, medicine and pediatrics should be represented at all times. The need for adequate staffing during evening hours and week-ends is imperative and studies are now in progress to see if the technique of computer simulation might eliminate the present guess work and determine optimum staffing patterns for an institutional emergency facility.

Until some new system for the delivery of emergency medical care is implemented, any institution planning a new emergency facility should pay close attention to available parking space. Though such a question may seem mundane it becomes important for the New Haven area when one considers that private automobiles are delivering 65% of the trauma patients to the Yale-New Haven Emergency Room. It is not unlikely that other area facilities are experiencing a similar situation. This creates problems for other vehicles arriving with seriously ill patients and can impede seriously their prompt attention.

Despite past and present emphasis by industry and public and private organizations on the importance of using safety devices, our data clearly establishes the fact that such devices are not being used even when they would have prevented or lessened the resultant trauma. Therefore, it seems apparent that such devices would be more effective if they were indeed "active" rather than "passive" in nature. In terms of automobile safety devices, from all available knowledge, the development of an ignition mechanism that would allow an automobile to be put into motion only after all safety devices were secure would reduce significantly the trauma from an injury-producing automobile accident.[15]

In the present study, information as to drug use, ingestion of alcohol and the patient's past medical history was felt to be too unreliable and hence discarded. Information regarding insurance coverage and third-party payment was felt to be meaningless without specific information regarding the nature and extent of coverage. However, we believe such factors as previous hospital admissions, past medical conditions, past injuries, and chronic conditions deserve further study. The relationship of such information to accidents and injuries would be important in the planning process of emergency medical services.

Summary

The concept of a Trauma Registry is proposed as a basic part of a methodology designed to study trauma and its relationship to emergency medical systems on a community, state-wide and institutional level. This concept is viable in pinpointing the prevalence of trauma and calculating its demand on the several components of any emergency medical care system.

The methodology employed in this study is effective enough to warrant its continued use, and we believe that its continued use will enable additional deficiencies and gaps in the present system to be identified as well as indicate promising areas for research into the diverse contributing factors of trauma. A physician should be in a position to provide community leadership in this area. It is doubtful that such leadership will be widespread without emphasis on the enormity of the trauma problem, attention to basic first aid procedures in the medical school curricula, and systematic education and experience in the handling of the traumatized patient.

The ultimate goal of this study is:

1. reduction of accidents and injuries with their medical, social and economic sequalae
2. development of a more effective community-wide emergency care system
3. prevention of accidents through an elimination of their contributory factors and better utilization of existing safety devices as well as the development of new ones
4. better patient care, teaching and research in the field of the trauma.

This research is supported in part by a grant from the Travelers Research Center, PHS Grant C1100037 from the Division of Community Health Services, Public Health Service and with assistance from the Connecticut Regional Medical Program.

This paper was presented at the Symposium on Automobile Accidents and Trauma, Yale University School of Medicine, March 5, 1969.

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THE PRESIDENT'S PAGE

Continuing Medical Education

Marks once stated that "the education of most people ends upon graduation; that of the physician means a lifetime of incessant study." What appeared to be a prophetic statement decades ago, is now axiomatic—"for the physician must forever be a student." What is of greater significance is that he must keep abreast of medical progress without neglecting his practice. No physician can afford to slight the everincreasing medical literature lest his colleagues, if not his patients, remind him of his shortcomings!

It appears incredible that any physician would ever question the need for continuing medical education or not take advantage of the effort of their local community hospitals to provide guest lecturers, seminars and symposia. His attention is directed to the superb, exhaustive study by Butler and Hage[1] who described the attempts and success of upgrading patient care in a community hospital through a program in medical education and who reported the findings of an investigation of the attitudes of the hospital staff to the changes introduced by the program. In short, "quid pretium eruditio medicinalis?"

In a recent pertinent study, the necessity for the physician to keep abreast of scientific advances was clearly expressed by Nemir.[2] Several pressures of increasing intensity now provide no choice for the physician but to continue his medical education in one way or another. First and perhaps the most significant pressure is "the knowledge explosion in the scientific world in depth and breadth." This is in great measure due to (1) the introduction of new specialties in medicine, with increasing fragmentation of the old, (2) the use of new basic tools and methods in the study of health and disease, and, very significantly, (3) the new organizational and socio-economic approaches to the delivery of medical care. One cannot help but add two other significant factors which add to the "educational pressure." The public is, without question, getting accurate, condensed, dramatized medical information almost "instantly." The public, thus, receives the facts perhaps even before the physician. The physician must be prepared even with data on organ transplants!

The second significant pressure affecting extended postgraduate education is concerned with the changes in the curriculum in medical schools. More and more, students are "accelerated"; more electives are offered; more specialization and "quicker" graduation are possible. Being of the old school, one cannot help but have second thoughts concerning medical acceleration, particularly in view of the many medical students who will later require educational redirection and training.

The third and last argument or pressure for continued medical education was recently particularly well expressed by Nemir as 'the stimulus it affords to a naturally inquiring mind, the pleasure of shared experiences with colleagues, the resultant ego satisfaction."

Those of you who have failed to get the message of this Page, read no further. Consider another profession, for you are slipping fast. However those of you, who agree that continuing education for physicians is mandatory and an inescapable obligation in order to provide optimum patient care, consult the latest compilation of "Continuing Education Courses for Physicians," printed in the JAMA, August 4, 1969.[3] The list includes 2,016 courses available at 525 institutions and organizations from Sept. 1, 1969 to August 31, 1970. This service is invaluable to physicians. It also serves as a voluntary system of accreditation for institutions offering such courses. The plan originated with an AMA Ad Hoc Committee in 1957 and has gained momentum steadily. What is particularly significant is that there is a *single, annual* list of courses available for physicians and, secondly, there has been a gratifying increase in participation not only by hospitals on a local basis, but also by medical specialties on a regional and national basis. No attempt will be made to analyze the success of these courses or to list the various modifications thereof instituted since 1957. Suffice it so say, this list is your primary obligation to your patients. It is your future "bread and butter."

Stevens J. Martin, m.d.

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SUMMARY OF PROCEEDINGS
HOUSE OF DELEGATES—SEMI-ANNUAL MEETING
New Haven, Conn.—December 11, 1969

MAJOR ACTIONS TAKEN

A. 1970 Budget

The budget for 1970, as prepared and submitted by the Council, was approved with one significant amendment. After considerable discussion, pro and con, it was VOTED to delete a $7,500 educational grant to COMPAC in 1970 and to allocate these funds to the Council to be used for political education activities among the membership as deemed appropriate by the Council. Membership dues will remain at the present $50 level.

B. Bylaw Amendments

Having been introduced and tabled at the 1969 Annual Meetings, a series of proposed amendments to the Bylaws were adopted as follows:

(1) To transfer the *Judicial Committee* from being a Standing Committee of the Council to being a *Standing Committee of the House of Delegates.* This action causes the Judicial Committee to be elected by the House, to report its actions to the House, and to obtain the endorsement of the House on any rule of ethics which the Judicial Committee recommends be made binding upon all members of the Society.

(2) To establish the office of *Vice-Chairman of the Council* and define the duties thereof.

(3) To abolish the *Committee on Medical Care of Veterans* and to transfer the functions thereof to the *Committee on Third Party Payments.*

(4) To change the name of the *Committee on State Blood Bank* to that of the *Committee on Organ and Tissue Transfers* and to expand the duties of the Committee to include keeping "abreast of developments in the field of organ and tissue transfers and the procurement, processing and preservation of organs and tissues used in such transfers" and cooperating "with interested agencies in the establishment and maintaining of high professional standards in the subject areas."

C. Reports

Council Report on CSMS-COMPAC Relations

It was VOTED to approve the Council's report on this subject, which, in brief, calls for the establishment of a new *Committee on Public Affairs.* Subject to adoption of appropriate amendments to the Bylaws (at the next meeting), the new Committee plus the Committees on National Legislation, State Legislation and Public Relations will make up a new "Public Affairs Division" (with deletion of the present Legislation and Public Relations Divisions). Meanwhile, approval of the report authorizes the Council to appoint a *pro tem* Committee on Public Affairs and designate the chairman thereof. The principal functions of the Committee on Public Affairs will be: (a) in cooperation with the Committees on National Legislation, State Legislation and Public Relations, to "plan a program of political education for the members of CSMS", such program "to be conducted on a year-round basis and be implemented by the office of the Executive Director; and (b) to maintain liaison with the Board of Directors of COMPAC and to encourage CSMS members to support COMPAC.

In addition, the report advocated that COMPAC "engage in an active voluntary membership drive" and that "future Directors of COMPAC be elected by the COMPAC Board of Directors on recommendations from County Medical Associations, selected from a list of COMPAC members in their respective Association areas to be furnished by COMPAC."

D. Resolutions

(1) *From the New Haven County Medical Association—Subject: Patient's Free Choice of Physician and Hospital:* It was VOTED to table the resolution and to place it on the agenda for the next meeting (May, 1970) for consideration and action.

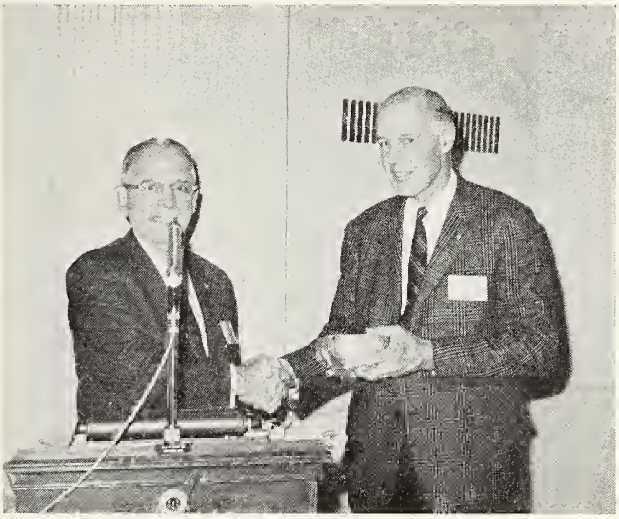
(2) *From the Litchfield County Medical Association—Subject: Physician Participation in Controlling Hospital Costs:* It was VOTED to adopt this resolution, calling for active encouragement of the membership to help control the costs of hospital care, and to refer the resolution to the Council for implementation.

E. Awards

Awards in recognition of service to the Society and its members were presented to the following recipients by Stevens J. Martin, President:

E. Awards

To Frederick C. Weber, Jr. Greenwich—for service as Secretary, 1968-69 (presented by Stevens J. Martin, President)



To E. Tremain Bradley, Norwalk—for service as Councilor-at-Large, 1968-69 (presented by Dr. Martin)

To Morris A. Granoff, New Haven—for service as Council member, NHCMA, 1967-69 (presented by Dr. Martin)

To William Mac Shepard, Putnam—for service as Council member, WCMA, 1963-69 (presented by Dr. Martin)

Also receiving awards *in absentia* were: *Richard F. Grant, Cromwell*—for service as Council member, MCMA, 1961-64, 1966-69; and *Hilliard Spitz, New London*—for service as Council member, NLCMA, 1963-69.

To Mrs. Josephine P. Lindquist, Associate Executive Director—in recognition "of her twenty-five years of outstanding service to the Society and of the valuable contributions she has made to its work and to its members." In addition, Mrs. Lindquist received a bouquet of roses and a commemorative gift. (presented by W. R. Richards, Executive Director)

FROM THE EXECUTIVE DIRECTOR'S OFFICE

William R. Richards, M.D.
Executive Director

160 St. Ronan Street, New Haven, Conn. 06511
Telephone 865-0587

Josephine P. Lindquist
Associate Executive Director

A Most Happy Occasion

At the semi-annual meeting of the House of Delegates on December 11, 1969, the serious and sometimes controversial business of the House was interrupted for a brief period so that the members could join together in paying spontaneous and sincere tribute to a member of the staff who has given twenty-five consecutive years of outstanding service to the Society—Mrs. Josephine P. Lindquist, Associate Executive Director. Because many of the Delegates have asked for copies of the presentation address, which was delivered by the Executive Director, the full text of the address is reproduced herewith:

"Our final award of the day goes to one who, characteristically, would deny being as deserving of recognition as the others, but whose record of dedicated service to the Society is second to none, and who—as you will note shortly— has the added distinction of being a great deal prettier.

"When our records revealed that 1969 marks a notable anniversary year for this very special recipient, I requested from our President—and was granted—the very special privilege of making this presentation myself. I am speaking, of course, of a staff colleague to whom I owe a great personal debt for her help and cooperation—Mrs. Josephine P. Lindquist, our Associate Executive Director.

"I find it very difficult to believe—and I am sure you do too— that Mrs. Lindquist could possibly be completing her twenty-fifth consecutive year as a member of the Society's staff, but that is exactly what she is doing. For anyone—in any field of endeavor—such an achievement is a memorable one in its own right,

"However, the deserved recognition we give this fine woman today is not merely in acknowledgement of the number of years she has devoted to Medicine's work. Rather, it is the kind of person she is—the continuing, self-prompted effort she has made to increase her capacity to assume and discharge ever greater responsibilities—that merits our heartfelt commendation on this anniversary occasion.

"Over her period of service, Mrs. Lindquist has been assigned many titles. Starting as a highly competent member of the secretarial staff, in the last ten years alone she has held, successively, the posts of Administrative Assistant, Assistant to the Executive Secretary, Assistant to the General Manager, Assistant General Manager, and—as I was pleased to report to the House a year ago—Associate General Manager. But even the latter designation proved to be short-lived in that, after only six months of getting used to, it had to be changed once again to that of Associate Executive Director.

"Be that as it may, I am confident that all of us will agree—just as we agree that a rose by any other name would smell as sweet—that a 'Good Jo' by any other name is still a 'Good Jo', and that we are indeed fortunate to have had this particular 'Jo' on our team for so long a time. I know, too, that all of us hope we can count on having her with us for a long time to come.

"And so, dear Mrs. Lindquist—dear Jo— it gives me great personal pleasure to present to you several tokens of the esteem in which you are held by our officers, the members of our Council and of countless committees, both past and present; by Connecticut physicians numbering into the thousands; and by many, many others who have benefitted from your good works and have had the privilege of your acquaintance.

"First, we offer you a bouquet of red roses as a symbol of our best wishes for continued good health, happiness and satisfaction in your work.

"Second, we award you this certificate, which reads: 'The Connecticut State Medical Society extends greetings to Mrs. Josephine P. Lindquist, and, with affection and gratitude, awards her this certificate in recognition of her twenty-five years of outstanding service to the Society and of the valuable contributions she has made to its work and to its members.'

"And finally, as a more material memento of this happy occasion, you are advised that arrangements have been made to have delivered to your home a television set—a fascimile of which, in living color, is mounted in this picture frame. You are instructed to ignore the fine print, lying immediately beneath the photograph, which informs you that your monthly payments won't begin until February; also, to understand that while you are hereby awarded custody of the set, your husband, John, is to be granted full viewing rights for the duration of the current football season. May it bring you both many hours of relaxation and entertainment."

W.R.R.

Placement Wanted

PREVENTIVE MEDICINE—54 years of age, Board certified wishes to associate full-time with college age people. Presently in practice. Would like to give three months notice.

INTERNIST—47 years of age, Board eligible wishes group or associate practice in Connecticut. Military obligation completed in Turkey. Available immediately.

ORTHOPEDICS-EMERGENCY ROOM—30 years of age with National Boards interested in an institutional or industrial type practice. Military obligation completed. Available immediately.

PATHOLOGIST—40 years of age, wishes solo or group practice in Connecticut. Presently in practice with military obligation fulfilled.

UROLOGIST—32 years of age, Board eligible wishes group or associate practice in Connecticut.

GENERAL PRACTICE-EMERGENCY ROOM—37 years of age wishes group or industrial type practice in Connecticut. Available immediately.

PEDIATRICIAN—39 years of age, wishes to practice in Connecticut. Available immediately.

PATHOLOGIST—34 years of age, with National Boards wishes to practice in solo, group or associate type practice in Connecticut. Military obligations completed. Particularly interested in sea shore location. Presently in practice.

SURGERY—35 years of age, eligible with National Boards wishes to practice in solo or associate type practice in Connecticut. Military obligations completed. Presently in practice. Particularly interested in sea shore location. Available immediately.

NEUROLOGY—29 years of age, eligible with National Boards wishes to practice in solo, group or associate type practice in Connecticut.

INTERNIST—38 years of age, Board eligible wishes to practice part time or full time position with hospital as Hematologist in Connecticut. Military obligations completed. Available immediately.

SURGERY—35 years of age, Board eligible wishes to practice in group or associate type practice in Connecticut. Presently in practice. Military obligations completed. Available immediately.

INTERNAL MEDICINE—GASTROENTEROLOGY—33 years of age wishes group or associate type practice in Connecticut. Will consider partnership in the Fairfield area. Eligible with National Boards. Military obligation completed.

SURGERY—32 years of age wishes solo or associate type practice in Connecticut. Military obligation completed. Eligible with National Boards. Presently in practice.

OBS & GYN—33 years of age wishes solo, group or associate type practice in Connecticut. With Connecticut license.

ANESTHESIOLOGY—34 years of age wishes solo type practice in Connecticut. Certified with National Boards. Presently in practice. Interested in directing a department of Anestheseology. Available immediately.

EMERGENCY ROOM—39 years of age wishes to practice in Connecticut. Passed National Boards. Military obligation completed in July 1970. Connecticut license.

SURGERY—36 years of age wishes group or associate type practice in Connecticut. Military obligation completed. Certified with National Boards. Presently in practice.

UROLOGY—37 years of age wishes institutional type practice in Connecticut. Interested in a full time academic post. Eligible. Presently in practice. Available immediately.

ANYONE INTERESTED IN THE ABOVE IS ASKED TO CONTACT THE PHYSICIANS PLACEMENT SERVICE, 160 ST. RONAN STREET, NEW HAVEN, CONNECTICUT 06511.

The Connecticut State Medical Society offers placement assistance through the Physicians Placement Service, 160 St. Ronan Street, New Haven, Connecticut, 06511. This service is for the use of physicians seeking locations, as well as physicians seeking associates, and is without charge.

Placement Opportunities

GENERAL PHYSICIAN—with interest in psychiatry. Part-time or contract to cover routine hospital services. Nights and/or weekends. For information write or call: Superintendent, Undercliff Mental Health Center, Meriden, Connecticut 06450.

STAFF PSYCHIATRIST—wanted full time or part time to direct therapeutic program in multidisciplinary team. Salary range $18,520-$23,755. Complete tax-free maintenance at nominal costs. For information write or call: Superintendent, Undercliff Mental Health Center, Meriden, Connecticut 06450.

PEDIATRICIAN—needed by small community in eastern Connecticut. Former pediatrician recently withdrew from practice to take fellowship training. Local hospital is well staff with specialists in various fields. Those interested in obtaining further information about this opportunity may contact: Edmond B. Raheb, M.D., Chief, Department of Obstetrics and Gynecology, Day Kimball Hospital, Putnam, Connecticut.

BOARD INTERNIST—for progressive 300-bed Hebrew Home for Aged, Chronic Disease Hospital License application in process, associated with large general hospital, medical school affiliation possible, salary negotiable. Send C.V. to: Benjamin E. Cohen, Chairman, Medical Conference Committee, The Hebrew Home, 615 Tower Avenue, Hartford, Connecticut 06112.

PHYSICIAN who will be willing to work on a salary basis for one or two years with an opportunity for subsequent full partnership after approximately three additional years. Practice consists of general-medical pediatric type practice with the exclusion of obstetrics and major surgery.

CHEST CLINIC PHYSICIAN—35-hour week. $18,-520-$22,846. Excellent fringe benefits. Training available as needed. Contact R. C. Edson, M.D., State Health Department, 79 Elm Street, Hartford, Connecticut 06115.

MEDICAL DIRECTOR—business equipment manufacturing concern. Well-equipped and staffed medical departments. Comprehensive occupational health program. Liberal fringe benefias. Salary negotiable. Contact Medical Director, Royal Typewriter Company, Division of Litton Industries, Hartford, Connecticut 06106.

GENERALIST OR INTERNIST—Growing central Connecticut residential community, fine schools, quiet country living. Twelve miles from 400 bed general hospital. For further information write or call William B. Lyons, M.D., R.D. #2, Kettletown Road, Southbury, Conn. 06488, Tele. 264-8884.

CONNECTICUT-PSYCHIATRIC RESIDENCIES—Community oriented, geographically unitized, mental hospital. Emphasis on Clinical Psychiatry. Training in Individual, Family and Group Psychotherapy. Expert supervision from senior faculty; affiliation with Yale University Medical School. AMA approved program, in a joint commission-approved hospital. Outstanding visiting lecturers. Automated records system and closed circuit T.V. Stipends: First year, $9323; Second year $9817; Third year, $10,694. Liberal benefits; housing available for a modest charge. Write to Mehadin K. Arafeh, M.D., Superintendent, Connecticut Valley Hospital, Box 351, Middletown, Connecticut.

VACANCIES FOR PART-TIME PHYSICIANS—Tours of duty are available to provide coverage on our Intermediate (Extended Care) Service evening, nights and weekends. Examples: 5:00 p.m.-8:00 p.m. (Weekdays)-$81.00 per tour; 8:00 a.m.-8:00a.m. (24 hrs. Sat or Sun. or Holidays)-$129.60 per tour. Interested physicians may make arrangements for intermittent or varying part-time tours of duty provided acceptable coverage is maintained during these periods. Part-time tours salary will be prorated according to above rates. Physicians must be U.S. citizens or possess permanent visas, and have licensure in one of the States. Write, visit or telephone: Chief of Staff, Intermediate Service or Personnel Officer Veterans Administration Hospital, West Spring Street, West Haven, Connecticut 06516—933-2561.

VACANCIES FOR FULL-TIME PHYSICIANS—Position open for Physician on Intermediate Service to provide supervision for rehabilitation and extended care for chronically ill patients. Physician must be U.S. Citizen or possess permanent visa, and have licensure in one of the States. Write, visit or telephone: Chief of Staff or Chief, Intermediate Service or Personnel Officer, Veterans Administration Hospital, West Spring Street, West Haven, Connecticut 06516—933-2561.

PEDIATRICS—Board certified or eligible wanted for association with Board man in a Connecticut shoreline community of 50,000. Close proximity to Yale Medical Center. Salaried first year, then partnership.

The Connecticut State Medical Society offers placement assistance through the Physicians Placement Service, 160 St. Ronan Street, New Haven, Connecticut, 06511. This service is for the use of physicians seeking locations, as well as physicians seeking assocates, and is without charge.

ANYONE INTERESTED IN THE ABOVE IS ASKED TO CONTACT THE PHYSICIANS PLACEMENT SERVICE, 160 ST. RONAN ST., NEW HAVEN, CONNECTICUT 06511.

Science News

Scheme For Medical Academy

Dr. James Shannon who retired a year ago as director of the National Institutes of Health and now based at the National Academy of Sciences is the chief instrument in planning a new academy, the National Academy of Medicine. He told the annual meeting of the American College of Physicians that there is a chance that the new academy of medicine will be functioning by the summer of 1970.

The intention is that the National Academy of Medicine should function as a spokesman for the interests of the medical profession and that it will operate as the National Academies of Science and Engineering have been doing by serving as a focus for public and government discussion.

There seems very little doubt that a suitably organized academy might bypass the AMA on most of the issues with which the medical profession is concerned especially in its academic branches. It might become the chief source of advice on the forward strategy for medical research and could at the same time exercise a decisive influence on the application of medicine in the community through programs such as medicare.

The origin of the new proposal seems to have been the work of a committee set up by the National Academy of Sciences in June 1967 to consider a range of medical questions. The intention seems to be that the new academy should be one of a troika organized along the patterns established by the academies of engineering and science and working closely with them.

Dr. Shannon's hope that the organization will be in being by 1970 may be fulfilled. It is hard to believe that the academy of medicine, not representing the medical profession will succeed in establishing a commanding role by then which it seeks without the practicing physician.—L.H.N.

Agent May Offer Protection For Heart Patients

(*JAMA*, 209: 352, July 21, 1969) Dr. Lester Morrison and his group at the Institute for Atherosclerosis Research at Loma Linda University have reported on the value of chondroitin sulphate, a mucopolysaccharide, on coronary heart disease patients. The mucopolysaccharide appears to have strikingly reduced coronary incidents such as acute myocardial infarction and ischemia in a group of heart disease patients who took the drug over a 2½ year period.

In 60 patients who took the drug there were 3 incidents, 2 fatal.

In 60 patients in a control group there were 28 incidents, 4 fatal. Apparently chondroitin sulphate (CSA) is antiatherogenic and antithrombogenic. The substance is found in connective tissue, nasal septa, trachea, and the arterial wall. It clears or reduces the lipid content of human cells including aorta and arterial tissues. CSA is prepared from bovine tracheal cartilage.

CSA was studied for its effect on plasma thrombus formation time in human subjects. The average time was 8.7 minutes in 17 patients with angina pectoris. After CSA the average was 11.7, 14.6 and 13.5 minutes after 30, 60 and 90 days respectively.

The substance is in short supply but when it becomes generally available there would be no contraindication to its use since it is taken by mouth and there are no side effects.—L.H.N.

Thirteen Years Later: Hybrid Antibiotics

(*Scientific Research*, 4: 17, August 18, 1969) A team of chemists and biologists at the University of Illinois have devised a way to produce hybrid antibiotics by changing the genetic structure of the microorganisms that produce them. The Illinois team produced four hybrids of neomycin which they call hybrimycin. Rinehart who headed the research explained the procedure used: "We started with Streptomyces fradiae the standard organism that makes neomycin and we caused the organism to mutate so it couldn't produce deoxy statamine a particular sub unit of neomycin."

Once they removed this product they fed the organism other related sub units, streptamine and epistreptamine and this procedure made new antibiotics. However, Rinehart cautioned that "we are very far away from marketable hybrid antibiotics." Nevertheless, they have uncovered a new method for making new antibiotics.—L.H.N.

Genetics And Laws Prohibiting Marriage In The United States

Farrow, M. G. and Juberg, R. C.: *JAMA*, 209: 534, July 28, 1969) In Georgia only of all the states a man is not prohibited from marrying his daughter or grandmother. All other political units prohibit marriage between a person and a sibling, an aunt or an uncle, and their prohibitions vary considerably for other degrees of collateral relationship.

The uncle niece marriage is not prohibited in Georgia and among Jews in Rhode Island. Generally marriages between persons with a coefficient of relatedness equivalent to first cousins or closer has been prohibited. Fewer than one-half of the political divisions have prohibitions regarding affinous marriages.—L.H.N.

The "Doctors Assistant"

(Coye, R. D. and Hansen, M. F.: *JAMA*, 209: 529, July 28, 1969) Practicing physicians in Wisconsin were surveyed to determine attitudes toward the concept of "doctors assistant," and the roles these assistants could fill in their practice. Only 32 per cent of the physicians responded! Of these 61 per cent believed that assistants are needed; 42 per cent stated they would use an assistant in their practice. Two types of assistants were identified.

The "hospital technicians" duties would be to serve primarily as an assistant in the hospital's surgical areas, the medical assistants duties would center in office practice settings and include taking medical histories, doing technical procedures and assisting with health supervision.

Existing programs train non-physician midwives, anesthetists, and "corpsmen." However, most responding physicians did not approve these duties for assistants.

Different groups of physicians had markedly differing ideas concerning appropriate responsibilities for assistants. In planning educational programs for such ancillary personnel, it seems highly desirable to recognize these varying attitudes.—L.H.N.

Self-Medication: Mirror Analysis Called Bad Psychiatric Therapy

(*JAMA*, 209: 497, 1969) Data on emotional illness among physicians are scarce. Physicians have a high suicide rate (36 per 100,000 compared with 11 per 100,000) in the general population. Dr. Bernard J. Baltes and Seymour Diamond noted in an AMA convention exhibit that physicians like other people often try to conceal emotional problems and seek help from non-psychiatric practitioners and turn to self-medication which can be dangerous.

Physicians should evaluate their colleagues emotional status at the time of routine examinations and when necessary recommend psychiatric help. Certain things in a physician's training may predispose him to depression. He is taught to control his emotions, go through long years of training in which emphasis is on details, conscientiousness and prolonged deferral of gratification. Any personal loss "may be enough to tip the balance towards a severe depression. Self medication makes matters worse, so does excessive drinking."

"The use of the narcotic or drug is initially justified by the physician because of some real or fancied physical complaint. In almost all cases, the drinking or the use of drugs represents a defense against intense anxiety feelings."

The exhibitors urge physicians to exercise enlightened compassion with regard to emotional difficulties in fellow physicians. The emotional problems of physicians need much more attention than they deserve.—L.H.N.

A Perspective On Medicaid

(Samuel Levey: *New Eng. J. Med.*, 281: 297, August 7, 1969) Most forecasts of Medicaid expenditures fell far short of actual costs primarily because of failure to develop realistic indicators of potential demand for health services by the needy and failure to account for expected increases in the cost of medical care.

For the year before the beginning of Medicaid of Massachusetts in September 1966 expenditures for medical assistance to welfare recipients were 107.6 million. Two years later costs for the same period were 205.8 million.

The largest component of Medicaid expense are in the hospital and nursing-home areas where price alterations are principally responsible for changes in costs. Few state Medicaid agencies have been able to impose meaningful controls upon the quantity and quality of medical care. In Massachusetts there will soon be inaugurated an automated data processing system to develop such information.

The capability of the states to offer comprehensive Medicaid services is unlikely until the health system undergoes major reorganization bolstered by greater federal participation through expanded matching funds.—L.H.N.

Aluminum Nicotinate Reduces Levels Of Serum Cholesterol

JAMA, 209: 353, July 21, 1969) At the Ninth Multidiscipline Research Forum, Dr. William P. Parsons, Jr. from the Jackson Clinic and Foundation, Madison, Wisconsin, reported on effect of aluminum nicotinate in 60 men and women afflicted by hyperlipoproteinemia. The drug promptly reduces the serum cholesterol levels of treated patients.

The first report of nicotinic acid's effectiveness in lowering serum cholesterol is now 15 years old. Because of severe side effects such as flushing and nausea it developed no popularity. However, when in the form of aluminum nicotinate it is absorbed with few adverse effects.

If the patient is simply overweight he needs only a reducing diet. But too much reliance on diet alone is generally not sufficient and drug therapy should be added. If a single drug fails to lower the lipid levels there are selected combinations of drugs to decrease the tendency toward coronary heart disease. —L.H.N.

Doctor's Office

Benito I. Bonaccorsi, M.D. announces the opening of his office for the practice of general surgery, 639 Highland Avenue, Waterbury, Connecticut.

William Cohen, M.D., and Melvyn R. Ostrov, M.D., announce the removal of their office from 83 Central Avenue to 475 Chase Parkway, Waterbury, Connecticut, 06708.

Arthur L. Delgrego, M.D., Carl V. Pantaleo, M.D., Harold D. Batt, M.D., and Charles M. D'Alessio, M.D., annouunces the removal of their office from 1441 Chapel Street to 301 Orchard Street, New Haven, Conn.

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X-Ray of the Month

Section of Chest Diseases

Arnold B. Rilance, M.D.

D.S. #73-24-29. A 34 year old Puerto Rican male, first seen in the Emergency Room of the Yale-New Haven Hospital on 9/26/68 complaining of acute symptoms due to bronchial asthma. Some 3 to 4 months prior, he had developed shortness of breath with wheezing. He made multiple visits to the Emergency Room between September and December of 1968. A psychiatric consultant made the diagnosis of Depression. He was hospitalized on three occasions between 12/24/68 and 1/28/69. On 3/25/69, he was seen in the Winchester Chest Clinics, at which time he was severely asthmatic. At a follow-up visit on 9/9/69, he appeared to be free of symptoms.

Discussion

The radiological diagnosis of anatomical emphysema is neither easily or accurately made. In the absence of bullous changes in the X-ray, one can only describe changes produced by overdistension of the lungs, which may or may not be due to anatomical emphysema, as illustrated in this case. Changes in the pattern of the pulmonary vessels may be helpful in making the diagnosis.

DR. ARNOLD B. RILANCE, Director, Winchester Chest Clinics, Yale-New Haven Hospital, New Haven.

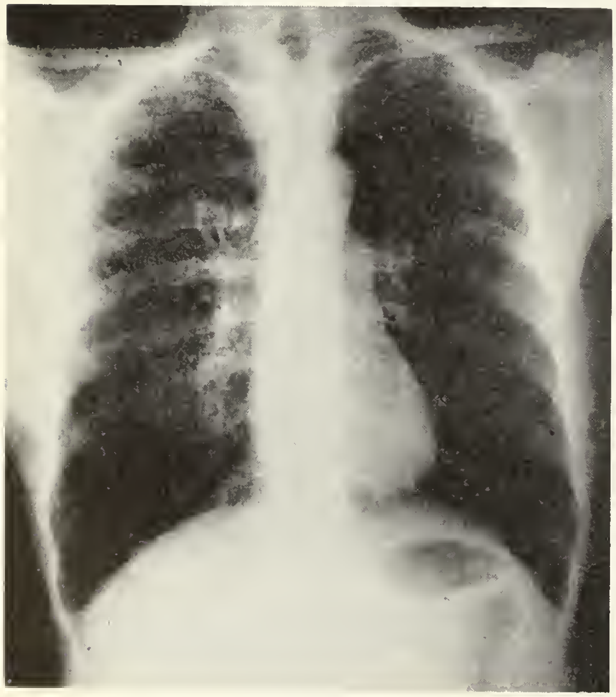

Figure 1

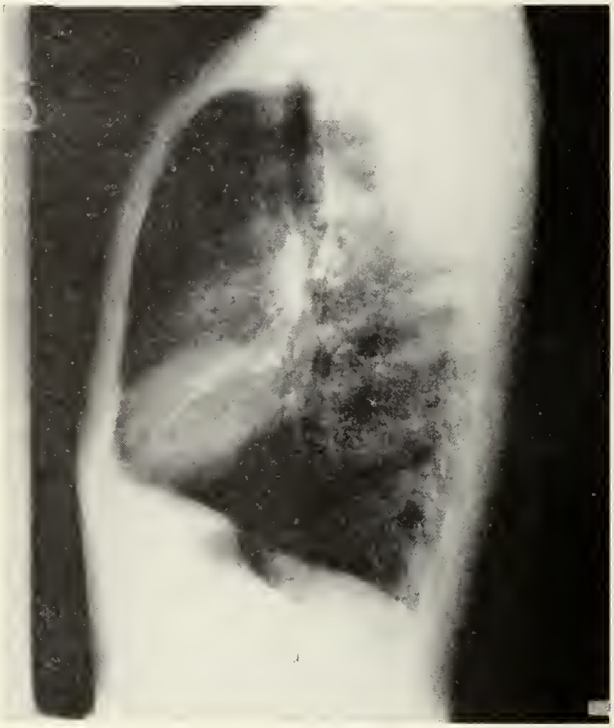

Figure 2

Figure 1 and 2. A conventional PA and lateral X-ray of the chest 3/25/69 (asthmatic) reveals changes due to over-distension of the lungs. Note flattening of the diaphragm, increase in diameter of retrosternal space, separation of the left ventricle from the diaphragm. There is increased prominence of the pulmonary artery conus. Scalloping of the leaves of the diaphragm is seen. These changes are all manifestations that are commonly interpreted as evidence of pulmonary emphysema.

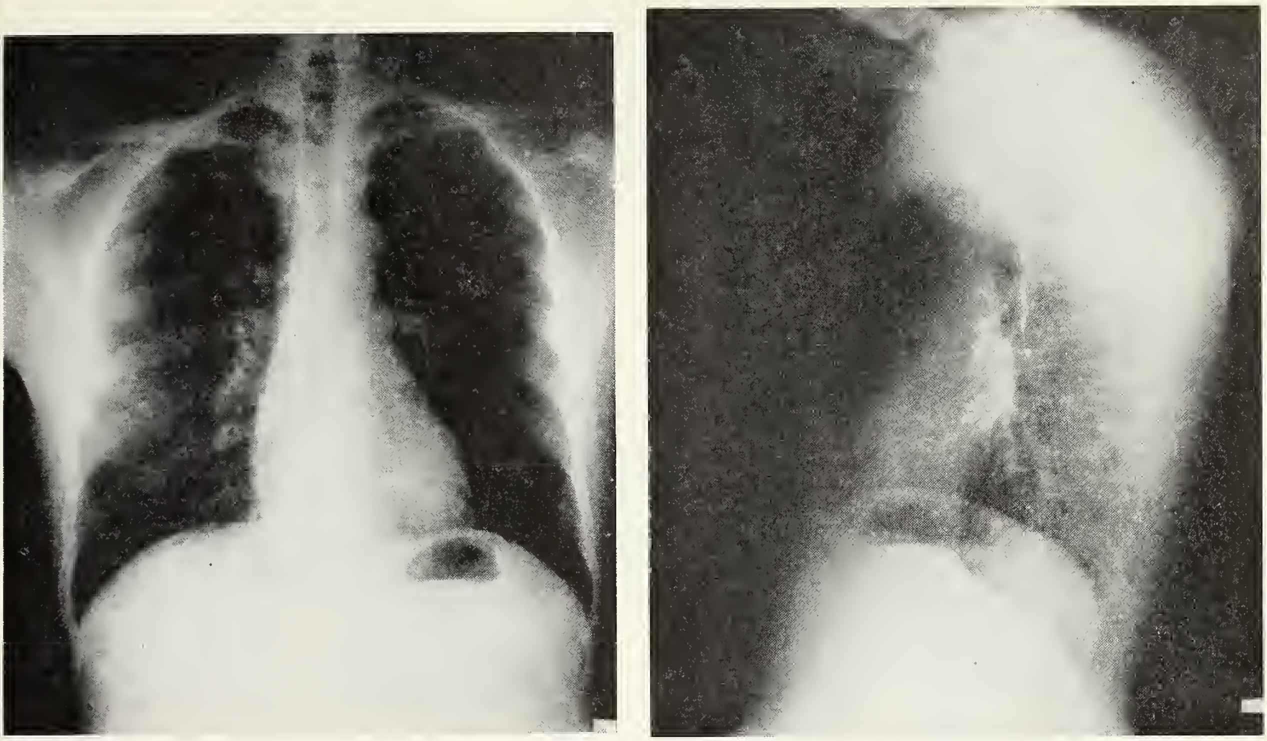

Figure 3 Figure 4

Figure 3 and 4. At a time when the patient is free of asthma, one sees loss of the pulmonary overdistension with normal vasculature and an appearance compatible with a normal lung.

Members of the Connecticut State Medical Society reading papers before other organizations are requested to submit their papers to the JOURNAL for consideration by the Board of Editors for publication. Please send them to:

Louis H. Nahum, M.D., *Editor*
CONNECTICUT MEDICINE
160 St. Ronan Street
New Haven, Connecticut 06511

By The London Post

British National Health Services

Part II

Ned Thomas

(This is the second of a series of six articles)

What benefits are British residents entitled to under the National Health Service?

Under the National Health Service Act of 1946, which was first proposed by the late Lord William Beveridge in his far-reaching report on social security in 1944, it was to be a comprehensive health service "designed to secure improvement in the physical and mental health of the people of England and Wales and the prevention, diagnosis and treatment of illness."

There are separate health acts for Scotland and Northern Ireland, but both of these are very similar to the one operative in England and Wales.

The total cost of the Health and Welfare Services in England and Wales for the 1968-69 fiscal year is estimated at slightly more than $3.7 billions, most of which is paid from taxes.

Revenue to support these services is also derived from individual weekly National Insurance pay,-ments, local taxes, and partial charges to patients for such things as prescriptions, glasses, dentures and dental treatment, and other sources.

When the National Health Service went into effect on July 5, 1948, ownership of 2,688 out of the then existing 3,040 voluntary and municipal hospitals throughout England and Wales came under the service. About 250 other hospitals, operated by various religious orders, remained outside of the service.

Most of the hospitals in existence then were old, some having been built in the 18th and 19th Centuries. Most of their equipment was antiquated. Starting gradually, hospital building under the National Health Service has steadily increased, gaining momentum in the last seven years.

In the first 10 years of the National Health Service, the sums spent on hospital construction renovations and new equipment averaged less than $24 millions a year. During the next five years (1958-59 to 1962-63), the amount spent on these improvements totalled $312 millions, for an average of $26 millions a year.

Since 1963, the amount of money put into building new hospitals has been rising markedly each year. During the past year a record $231.6 millions has been put into new hospital construction.

The vast majority of general and special hospitals in the country, covering every conceivable type of treatment, are available to treat sick persons who need hospitalization under the National Health Service. They provide both in-patient and out-patient care in every kind of hospital, including pychiatric hospitals.

Great Britain's hospital service is organized on a regional basis. To keep hospitals abreast of the latest development, each region is associated with a university having a teaching hospital or medical school.

People in Great Britain have been receiving a steadily increasing amount of hospital care, as evidenced by the following statistics:

The population of England and Wales increased from 45.1 millions in 1958 to 48.4 millions in 1967, an increase of 7.3 per cent. Over the same period, the number of in-patients treated in National Health Service hospitals rose from 3.9 millions in 1958 to 5 millions in 1967, an increase of 28 per cent.

The number of out-patients seen in departments other than accident and emergency in 1958 was 7.1 millions and in 1967 the number had jumped to 7.9 millions, an increase of 11 per cent. Out-patients seen in accident and emergency departments rose from 5 millions in 1958 to 7.4 millions in 1967, an increase of 48 per cent.

Nearly all of the country's more than 10,000 specialist and consulting doctors participate in the

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MR. NED THOMAS is a science medical writer for the New Haven Register on leave.

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Cough Suppressant		●	●		●
Antihistamine			●		
Long-Acting (6-8 hours)		●			●
Nasal, Sinus Decongestant				●	
Non-narcotic	●	●		●	●

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hospital service, either full-time or part-time. Their services are free to National Health Service patients.

The part-time specialists are free to take on private patients, and about one per cent of all the hospital beds in the country are set aside for private patient use.

Patients who enter a hospital under the National Health Service enjoy free treatment and maintenance. However, patients who desire privacy, which may not be considered necessary on medical grounds, may be given such accommodations but they have to pay private rates for them.

The majority of doctors in the National Health Service work in partnerships with other doctors or in group practice. In either case, a doctor or any of his partners may have up to 4,500 patients on his individual list so long as the average of the combined National Health Service lists in the group or partnership does not exceed 3,500.

A doctor who prefers to work alone may have up to 3,500 patients on his National Health Service list. The average list for the country is about 2,500.

There is a complex formula for remunerating a doctor under the National Health Service. Included in the formula are a basic allowance, allowances for the size of a doctor's list, special allowances for seniority, group practice, practice in designated areas where there is a shortage of doctors, specialization training, payments for night visits, for treating persons over 65 years of age, and out-of-hours responsibilities including a supplementary practice.

Everyone enrolled under the National Health Service is entitled to medicine and certain specific appliances at drastically reduced rates.

A patient who receives a prescription from a doctor in the service may present it to any one of about 14,000 drug stores or suppliers of appliances participating in the National Health Service. Regardless of the cost of the medication the patient pays a fixed charge of only 30 cents for each prescription.

No charges are made for medicine prescribed for: children under 16 years of age, people who are 65 years or older, expectant mothers, mothers of a child under 12 months of age, and people who suffer from a special medical condition which is certain to require continuous medication for long periods.

Any person who resides in either England or Wales is entitled to receive under the National Health Service "all the treatment he needs to make him dentally fit" so that he can enjoy "a reasonable standard of dental efficiency and oral health as is necessary to safeguard general health."

No charge is made for the clinical examination of a patient's mouth. Repairs to dentures are also free, but there is a charge of $2.50 for treatment, or the full cost of any treatment if less than $2.50.

A big saving occurs when a patient needs to have full upper and lower dentures made. He only has to pay about half the full cost subject to a maximum, including other treatment, of $14.50.

There is no charge for dental work on: expectant mothers, mothers who have had a child in the preceding 12 months, children under 16, or 16 or over but still in full-time attendance at school. Other patients between 16 and 20 pay only charges for dentures.

Dentists are free to take part in the service if they wish. They may practice in any area they choose and may have private patients as well as patients who come under the National Health Service. The majority of dentists (about 10,400) in the country participate in the service.

Eye examinations are free, but if glasses are supplied the patient has to pay $2.40 for bifocal lenses and $1.50 for other lenses, plus the cost of the frame. Children under 16 do not pay for glasses, nor do children over 16 if they are attending school full-time.

(The third report in the series, discusses the Conservative Party's view on the National Health Service.)

LABORATORY NOTES

Malaria

Norwalk is not generally considered a tropical disease center but in October 1969 we found 2 cases of vivax malaria (Vietnam veterans) and 1 case of severe falciparum malaria (pilot, Africa). Because the parasites may be scarce and hard to find it is important for the clinician to suspect the disease and order "smear for malaria" specifically.

CSF Electrophoresis

Since normal CSF has 0.5-1% of the protein concentration of serum, the protein of CSF must be concentrated 100-200 times before electrophoresis. We have recently switched to vacuum ultrafiltration (dialysis across a collodion membrane, with the dialysis fluid under vacuum). The method gives the most accurate results in the critical gamma globulin range. A minimum sample of 7-10 ml is required.

The electrophoretic pattern resembles that of serum except for the presence of a pre-albumin fraction and a lower proportion of gamma globulin in CSF. The proportions of the protein fractions, not their actual concentrations, will be reported. Up to 14% gamma globulin is normal, 14-16% borderline, and above 16% elevated. An elevated proportion of CSF gamma globulin has been noted in *active multiple sclerosis,* with or without an elevated total CSF protein concentration. However, the changes are not specific (elevations of CSF gamma globulin may also be seen in inflammatory diseases of the CNS and in intracranial tumors), and false negatives are common. A non-specific rise in the CSF gamma globulin fraction may occur when the serum gamma globulin is elevated, so it is advisable, in case an elevated proportion is reported, to rule out this possibility by obtaining a serum electrophoresis.

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2. Kaplan, A. and Johnstone, M.: Concentration of Cerebrospinal Fluid Proteins and Their Fractionation by Cellulose Acetate Electrophoresis. *Clin. Chem.* 12:717-727, 1966.

Signed: S. Winter, M.D.

Sweat Test

We recently performed a sweat test for sodium and chloride and obtained only .003 mg of sweat after iontophoresis instead of the minimum of .03 mg we need for analysis. On repeat a week later the same thing happened. The diagnosis of congenital ectodermal dysplasia with inability to sweat had been suspected on clinical grounds (family history) and was confirmed in this somewhat unusual fashion!

Lipid Metabolism

As a supplement to our June 1969 issue on lipids we add the following information.

We now perform triglyceride tests so that our available "lipid profile" consists of inspection for chylomicrons; cholesterol; triglycerides and lipoprotein electrophoresis. These tests may also be ordered individually.

We do not perform total lipids or phospholipids; these tests are not currently considered of any importance except for research. (Puckett, ASCP Clin. Chem. CC 58, Aug. 1969).

Packed red cell use

For the year 7/1/68 to 6/30/69 approximately 30% of all red cells transfused in Connecticut were administered as packed red cells and 69 as whole blood. For Norwalk Hospital the figures are 25% and 75%. For most purposes packed cells are as good or better than whole blood and we urge you to use them when possible.

Reference Lab.

We currently serve as a reference laboratory for the National College of Pathologists Survey and for the states of Pennsylvania and Conn.

Sorbitol

We are now carrying 1.5% sorbitol rather than 1.5% glucose peritoneal dialysis fluid. Main advantage is that sorbitol is less acid after autoclaving and causes less discomfort.

ROY N. BARNETT, M.D., Norwalk Hospital, Norwalk, Connecticut.

Electrocardiogram of the Month

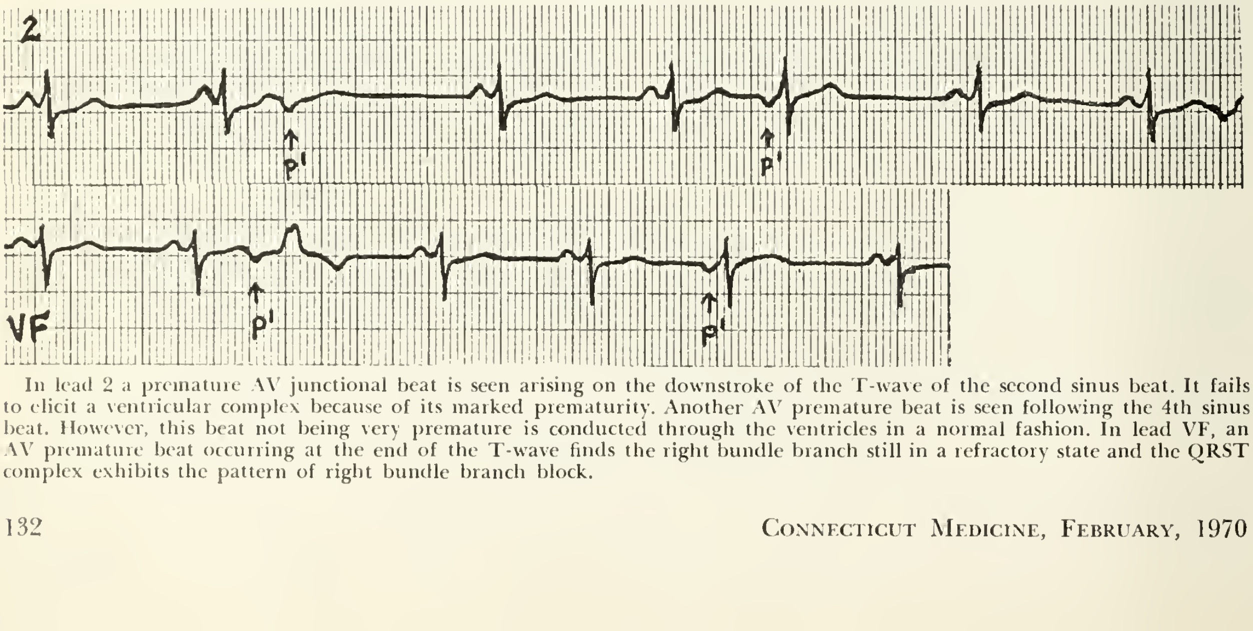
Yale-New Haven Hospital
New Haven, Connecticut

Prepared by
HYMAN M. CHERNOFF, M.D.
Associate Professor of Clinical Medicine,
Yale School of Medicine
Director, Dept. of Electrocardiography
Memorial Unit, Yale-New Haven Hospital

Because of possible therapeutic implications, it is important to differentiate premature beats of supraventricular origin from those of ventricular origin. In most instances this is not difficult since in the case of atrial premature beats an ectopic P-wave can be seen preceding the early ventricular beat and the configuration of the QRST complex is similar to that of beats of sinus origin in the same lead. When the premature beat is of ventricular origin, no ectopic P-wave precedes it and the configuration of the QRST complex differs from that of beats of sinus origin. At times, however, the ectopic P-wave may not be easily seen or in the case of premature beats of AV junctional origin the ectopic P-wave may be buried in the ventricular complex. Such premature beats can still be identified as of supraventricular origin if the configuration of the QRST complex of the premature beat resembles that of the sinus beats recorded in the same lead. This, of course, will only happen if the premature supraventricular beat arrives at the ventricular conducting system at a time when it is no longer in the refractory state and can conduct the excitation wave in its usual manner. A supraventricular beat, however, may be so premature as to arrive in the absolute refractory period of either the Bundle of His or of all of its three branches (the right bundle, the anterior (superior) division of the left bundle, and the posterior (inferior) division of the left bundle) and it will, therefore, not elicit a ventricular response. Should a supraventricular premature beat arrive at such a time as to find one or two of the three conducting branches still refractory to conduction, the excitation wave will be initially conducted through the ventricle along the bundle or bundles that are no longer refractory. This aberrant spread of the excitation wave through the ventricles will thus produce ventricular complexes which simulate the patterns resulting from premature beats of ventricular origin. Their true identity as premature beats of supraventricular origin will depend upon a careful search for a preceding ectopic P-wave.

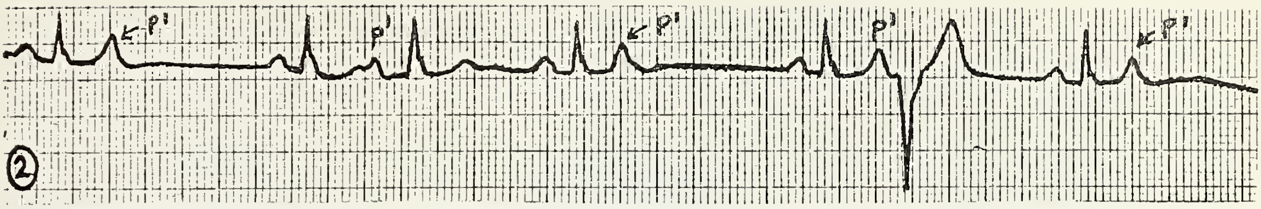
Below are a number of examples in several patients of the effect of the degree of prematurity of premature supraventricular beats upon the configuration of the QRST complex. The form which the aberration takes is determined by which of the bundles are still in a refractory state when the excitation wave arrives in the ventricular conducting system.

Figure I



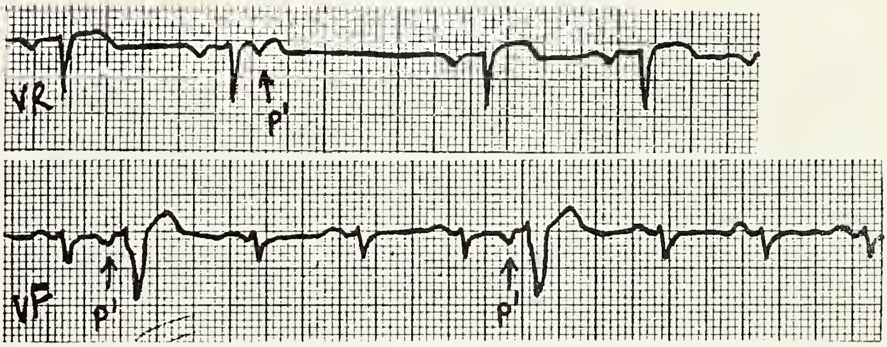
In lead 2 a premature AV junctional beat is seen arising on the downstroke of the T-wave of the second sinus beat. It fails to elicit a ventricular complex because of its marked prematurity. Another AV premature beat is seen following the 4th sinus beat. However, this beat not being very premature is conducted through the ventricles in a normal fashion. In lead VF, an AV premature beat occurring at the end of the T-wave finds the right bundle branch still in a refractory state and the QRST complex exhibits the pattern of right bundle branch block.

Figure II



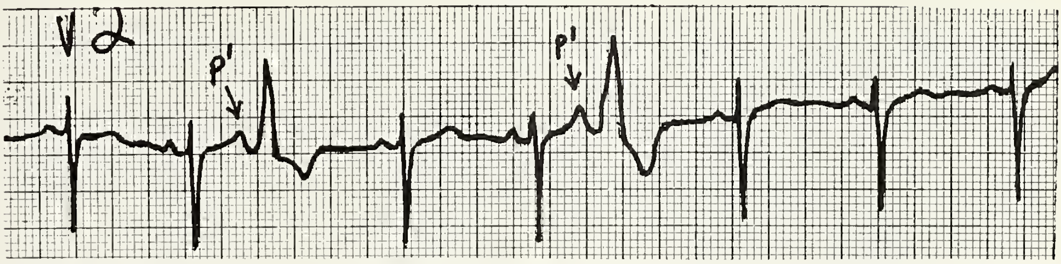
In this lead 2 there are five premature atrial beats. The first APC occurs during the apex of the T wave of the first sinus beat. Because of its marked prematurity it finds the entire bundle system refractory and is not conducted to the ventricles. The second APC occurs on the downstroke of the T wave of the second sinus beat and is conducted in a normal fashion. The third APC follows the third sinus beat, but is not conducted. The fourth APC arises at the apex of the T wave and is aberrantly conducted through the ventricles exhibiting patterns of left bundle branch block. The fifth APC being very premature is not conducted to the ventricle.

Figure III



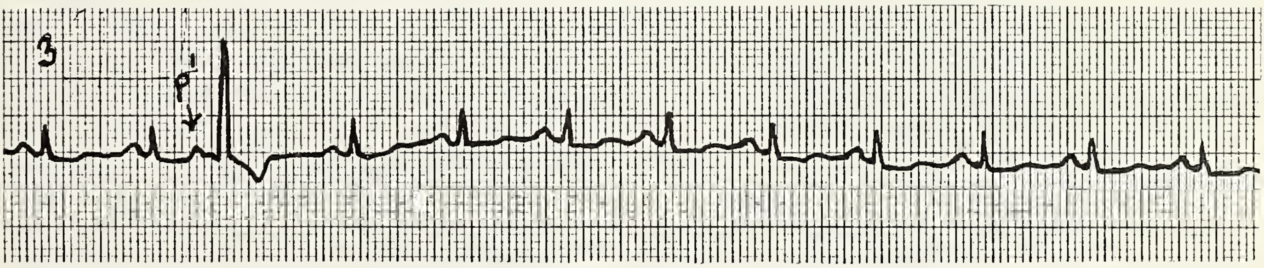
In lead aVR an APC occurs during the middle of the ST segment of the second sinus beat and because of such marked prematurity it fails to be conducted to the ventricle. In lead aVF an APC follows the first and fourth sinus beats. Being somewhat less premature they are conducted to the ventricles but with aberrancy, exhibiting patterns of left bundle branch block.

Figure IV



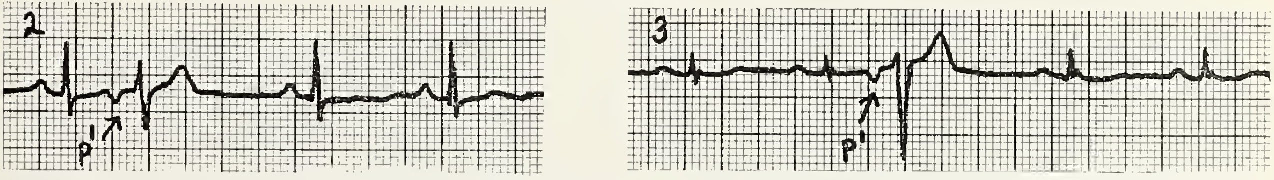
In this lead V2 there are two APCs which are conducted to the ventricles in an aberrant fashion, exhibiting patterns of right bundle branch block.

Figure V



One APC is seen in this lead 3. It occurs at the end of the T wave of the second sinus beat and exhibits patterns characteristic of delay in conduction in the posterior (inferior) division of the left bundle branch.

Figure VI



In leads 2 and 3 there are APCs which by virtue of their degree of prematurity find the anterior (superior) division of the left bundle branch still in its refractory period. The ventricular complexes therefore exhibit abnormal left axis deviation.

WOMAN'S AUXILIARY

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The eastern regional workshop of the Woman's Auxiliary to the AMA was held at the Sheraton Park Hotel, Washington, D.C. last October. It opened with a luncheon presided over by Mrs. Herbert Ulrich, eastern regional vice-president. Our eastern region consists of the following states: Connecticut, Delaware, District of Columbia, Maine, Maryland, Massachusetts, New Hampshire, New Jersey, New York, Pennsylvania, Rhode Island, Vermont, Virginia, West Virginia. Dr. R. T. Holden, member of the AMA board of trustees, spoke to members and national officers after lunch. Our national president, Mrs. John Chenault then introduced the committee chairman: membership—Mrs. G. P. Lee, AMA-ERF—Mrs. Howard Ellis, Children and Youth—Mrs. Paul Rauschenbach, Health Careers—Mrs. Wendell Roller and Legislation— Mrs. William Flood, presidents-elect—Mrs. R. C. Robertson. These six discussion groups met for the afternoon in their own groups.

The presidents-elect learned at their round-table discussions the duties of their job. 1. *visit the counties in your state and nearby states before becoming president. Attend the national and workshop meetings.* 2. *know parlimentary procedure—Three parlimentary pointers to promote*:

a. sign reports or minutes with name and office never "respectfully submitted"

b. never say "old business" but "unfinished business"

c. never say 'turn the meeting over" say "the program chairman will take charge at this time"

3. *have tools necessary for job*
a. leaders handbook
b. president's book
c. orientation book

Have a system worked out for all officers and chairman to hand over their books. One officer can be appointed to collect them and then hand the books out to the new officers at one time. Have the duties of the job passed on with the books.

4. *Picking state board chairman*—consider plan to have a form for each county to send names of members who would be good chairmen—points to consider in choosing chairman—a. talent for job; b. congenial person; c. good health; d. children's ages and husband approval; e. potential for leadership. Do read annual reports at the annual meeting—don't just pass out reports!

5. Each state sends in a blue form for a national representative to attend their annual meeting. Please send the form in early and tell national what your state expects—a speech, to address the men's house of delegates, or she could install the new officers. November 1st is always the deadline for the President to recommend a person for regional or national office. (remember a regional chairman need not have been a state president).

New ideas for Presidents-elect—

1. invite other organizations to "good meetings".
2. work with other organizations on projects.
3. discussion was held on how counties relate to state—do state chairman contact the county chairman? do they want to work with the state or just their own town?
4. instead of one workshop have the chairman from the regional workshop travel to each county workshop.

An informal dinner was held that night for the whole group. The program was "Leadership and Parlimentary Procedure". The next morning started in early with a discussion group meeting at 8:00 combined with a continental breakfast. From Connecticut those attending were: Mrs. Edwin Trautman from Fairfield County, AMA-ERF chairman, Mrs. Ronald Beckett from Hartford County, Legislation chairman, Mrs. Raymond Zagraniski from New Haven County, Community Health, Mrs. William Richards from New Haven County, Health Careers, Mrs. Noah Barysh from Litchfield County, Membership Chairman, and Mrs. John Mendillo from New Haven County, President-elect. The rest of the day until adjournment at 3:00 P.M. was spent in the committee discussion groups.

Mrs. Frank Gastineau explained to each group the new package program called "One Dozen Days". As the government is already so involved in medicine, we should encourage our auxiliary members to be politically active, work on school boards, PTA, bond issues, drug abuse, air and water pollution committees, etc. Now, more than ever, involvement in public affairs has become a vital responsibility on the part of every intelligent, concerned American citizen. Realizing the importance of this involvement, the AMA Division of Public Affairs is asking for our assistance in improving and expanding activities in this area. We are not being asked to do something new. It is well know that a large number of our members have been, and are now engaged in public affairs projects within our communities. We are being asked to continue our efforts, enlarge our efforts, help motivate other members to become involved, and to do this in a cohesive, well-defined way that will alert our communities that medicine is concerned about communal problems. The use of this project will be the decision of each county auxiliary.

Our AMA representative is Mr. Ed Donlan. The AMA has realized that they must change their image and they are employing people to help do this. We should call on Mr. Donlan and our three advisors here in Connecticut to come and talk with us. There is also a new more relaxed attitude from the National Auxiliary. In some counties, in several states in the east, the members want to meet socially and do not care to "work on projects". If that is what the members want to do—let them! But we hope here in Connecticut that we still have our "workers". Connecticut was well represented at the Washington regional meeting and those attending came back with a new enthusiasm.

Georgine Mendillo
President-Elect

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The 186th Annual Meeting of the New Haven County Medical Association will be held on Thursday, March 19, 1970 at the Waverly Inn, Cheshire. The Business meeting will start at 3:00 p.m.

The business meeting will be followed by the 17th Annual Joint Dinner with the Woman's Auxiliary to the New Haven County Medical Association. At this time the presenting of the Association Plaque to the Past President will be held.

Date: Thursday, March 19, 1970
Place: Waverly Inn, Cheshire
Time: Business Meeting—3:00 p.m.

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OBITUARY

Eugene M. Blake, M.D.
1882-1969

It is strange but perhaps part of death's choice to sometimes make a final call years after the reputation and personality of an individual is best known. This was the case with Dr. Eugene M. Blake who died on Sunday, December 28, 1969.

Dr. Blake was a gentleman, loved by his family, patients and colleagues. Best known for his cataract and glaucoma surgery, in his later years he elected to specialize in glaucoma.

After getting his medical degree at Yale in 1906, he served on internship in the Hartford Hospital, and joined the staff of the Yale Medical School in 1907 and became a clinical assistant in 1908 and an instructor in 1910. His service at the medical school was interrupted only by a period of military service in the First World War when he was a Captain in the Army Medical Corps. During the Second World War he was Chief of the Eye Panel at the New Haven Induction Center.

When Vice President for the National Association for the Prevention of Blindness in 1947 Dr. Blake campaigned for the establishment of a national foundation to study and finance the treatment of glaucoma. He said the nation needed a foundation to function like those operating in the field of cancer, infantile paralysis and heart disease.

In 1938 Dr. Blake was named state supervising ophthalmologist for a Connecticut program for aiding the blind. He contributed freely of his time to hospitals and welfare agencies. He was a member of the National Committee for British Relief during the Second World War and in 1944 was chairman of American Relief for Italy in the greater New Haven area.

Dr. Blake was clinical professor of ophthalmology from 1923 and head of the department from 1935 until his retirement in 1951, after 44 years on the staff of the Yale University School of Medicine. He was considered one of the nation's foremost opthalmologists and in 1967 received an award from the Connecticut Society for the Prevention of Blindness which he helped found 15 years earlier.

One of Dr. Blake's outstanding contributions was his paper "The Effect of ACTH in Glaucoma", published in the *American Journal of Ophthalmology*, 33:1231, 1950. This was one of the first papers, pointing out the possible connection between cortisone and glaucoma.

Dr. Blake served as a governor of the American College of Surgeons; past president of the American and New York Ophthalmological Societies; Yale Alumni in Medicine, and New Haven Medical Association and was a member of the American Medical Association, New York Academy of Medicine and the Connecticut State Medical Society.

Besides his wife, Mrs. Ruth Sexton Blake, he leaves a daughter, Mrs. Carabella Blake Neil of Flanders, New Jersey and two granddaughters.

R. M. Fasanella, M.D.

In Memoriam

BUCKLEY, JOHN W.,— Bridgeport, Georgetown 1933. Dr. Buckley was chief of pediatrics at St. Vincent's Hospital for 15 years. He joined the staff of St. Vincents' Hospital in 1935. Dr. Buckley was president of the St. Vincent's medical staff in 1950 and held a variety of posts on the staff including program chairman of the annual banquet more than 20 years. During World War II, Dr. Buckley served with the U.S. Public Health Service. He was a member of the Hezekiah Beardsley Pediatric club of Connecticut, American Academy of Pediatrics, New England Pediatrics society, American Public

Health Association, American Medical Association, Fairfield County Medical Association and the Connecticut State Medical Society. Dr. Buckley died December 26 at the age of 63.

CONROY, MICHAEL J.,—Meriden, Yale University School of Medicine 1920. Dr. Conroy was a surgeon in the Meriden area for many years before his retirement. He was on the staff of the Meriden Hospital. Dr. Conroy was a member of the American Medical Association, New Haven County Medical Association and the Connecticut State Medical Society. Dr. Conway died December 10 at the age of 73.

LARRABEE, JOHN W.,—West Hartford, Harvard Medical School 1926. Dr. Larrabee was an orthopedic surgeon in the Hartford area before his retirement in 1958. He had been chairman of the medical staff of Newington Home and Hospital for Crippled Children and had been on the orthopedic staff at Hartford Hospital. He was also on the staff of the McCook Hospital. He was elected president of the Connecticut Rheumatism Society in 1955. Dr. Larrabee was a member of the American Medical Association, Hartford County Medical Association and the Connecticut State Medical Society. Dr. Larrabee died December 28 at the age of 74.

LOMBARDI, PASQUALE F.,—Waterbury, Tufts 1921. Dr. Lombardi was a general practitioner in the Waterbury area for many years. He was on the staff of the Waterbury Hospital and St. Mary's Hospital. He was attending physician at the Chase Metal Company. Dr. Lombardi was a member of the American Medical Association, New Haven County Medical Association and the Connecticut State Medical Society. Dr. Lombardi died December 19 at the age of 79.

SENFIELD, MAXON M.,—Derby, University of Vienna 1920. Dr. Senfield was a general practitioner in the Derby Ansonia area for 45 years. Dr. Senfield was just reappointed a staff member at the Griffin Hospital, a post he has held for a number of years. He was a member of the American Medical Association, New Haven County Medical Association and the Connecticut State Medical Society. Dr. Senfield died January 6 at the age of 74.

ZWICK, FRANK,—New Britain, University of Vermont 1913. Dr. Zwick was a surgeon in the New Britain area for many years. Dr. Zwick was the first doctor to serve his internship at the New Britain General Hospital in 1913. He was engaged in private practice here from 1914 until his retirement in 1968. He was a former chairman of the New Britain Board of Health and was examining physician of the fire department. Dr. Zwick was a Navy veteran of World War II. Dr. Zwick was a member of the Hartford County Medical Association and the Connecticut State Medical Society. Dr. Zwick died December 22 at the age of 80.

MEETINGS

GENERAL

May 12, 13, 14

178th Annual Meeting

Connecticut State Medical Society

Hartford-Hilton Hotel, Hartford

MEDICINE

Weekly Oncology Courses **12 Noon**

Hospital of St. Raphael, Radiation Therapy Conference Room

February 12

Bone Marrow and Tissue Transplantation, Malcolm S. Mitchell, M.D.

February 19

Case Presentation

February 26

Carcinoma of Prostrate, John B. Goetsch, M.D.

Peter Bent Brigham Postgraduate Medical Series

March 13 **8:30 A.M.-5:30 P.M.**

Diabetes Mellitus: Clinical Management, George Cahill, M.D., Director, E. P. Joslin Laboratory

SURGERY

March 7

11th Annual Postgraduate Anesthesia Seminar

New Jersey State Society of Anesthesiologists

Cherry Hill Inn, Cherry Hill, N.J.

Registration fee (including lunch) $14.00 to nonmembers; interns and anesthesiology residents admitted free

May 6, 7, 8

43rd Annual New York Eye and Ear Infirmary Clinical Conference

Biltmore Hotel, New York City

Held in conjunction with the 150th anniversary celebration of the New York Eye and Ear Infirmary. An open house will be held at the New York Eye and Ear Infirmary on Saturday, May 9, featuring scientific exhibits and demonstrations of newer instrumentation and techniques.

Contact Jane Stark, Executive Secretary, 310 East 14th Street, New York, N.Y. 10003

AROUND THE STATE

New Haven County

No association meetings were held prior to the January 10th deadline for this month's *Journal* publication, although the Executive Committee has been meeting regularly since early December. Th executive committee, along with several association members on an ad-hoc basis, is studying problems in the areas of public relations, by-laws changes, compulsory attendance management, review committee logistics, and general organization.

The following material which is used by the New Haven County Medical Associations' Committee on Credentials and Orientation for the indoctrination of new members is reprinted with the thought that it might be of general interest.

"SEVEN UNDERSTANDINGS" ABOUT NEW MEMBERSHIP

I. Each new member should understand that organized medicine is a constitutional form of democratic self-government based upon proportionate representation and guided by the one-man, one-vote principle.

Every licensed physician is eligible to join the smallest unit of organized medicine, namely the "County Medical Association". He may come twice each year to a county meeting open to all of the membership to express an equal voice and equal vote in determining the association's entire policy. Special meetings of the association can be called whenever necessary under rules set forth in the by-laws.

Between these meetings, authority is placed in the hands of his duly and proportionately elected executive committee, called in New Haven County, "The Board of Governors".

The next largest unit, the "Connecticut State Medical Society", consists of all licensed physicians in Connecticut who have already joined one of their eight component county associations. However, because of its size—over 3,800 members—the state society is, of necessity, governed by a representative system similar to our United States House of Representatives. For every 35 members enrolled in each county association, that association is entitled to 1 delegate to our State House of Representatives, called "The House of Delegates". The House of Delegates meets twice a year and each individual delegate has an equal voice and an equal vote in determining the state's policy.

Between meetings, authority is placed in the hands of the duly and proportionately elected executive committee, called in Connecticut, "The Council".

The largest unit, "The American Medical Association" or "AMA", consists of the members of the county and state medical societies throughout America, is governed by a similar representative system, called "The A.M.A. House of Delegates" which, likewise, meets twice a year.

Between meetings, authority is placed in the hands of the duly and proportionately elected executive committee, called "The Board of Trustees of the AMA".

Thusly, every licensed physician in Connecticut and in America is entitled to his own voice and his own vote in equal share with all other physicians from the bottom to the top of the ladder of medical self-government. . . . . To use or not to use this voice and vote should be a matter of thoughtful reflection on the part of each new member.

II. Each new member should be informed that the Connecticut State Medical Society and the New Haven County Medical Association as well as certain local societies maintain varied and extensive Group Insurance Programs for the benefit of the membership. Details can be obtained from the offices of the organizations and prompt investigation of the merits of these plans should be made by each new member.

III. Each new member should plan to join a specialized scientific section of the Connecticut State Medical Society according to the Specialty Section of his own choice. The details are spelled out in a publication by the Connecticut State Medical Society available through that office.

IV. Each new member is enjoined not to sign blank prescriptions, no matter how convenient, as such action is against every medical society policy. All offenders are subject to discipline by the Department of Health in Hartford.

V. Each new member should report actual, threatened, or suspected cases of malpractice suits to his insurance carrier and to his "Committee on Medical Ethics and Deportment" of the New Haven County Medical Association as promptly as possible. Failure to do so, may cause unneeded distress on the part of not only the member, but all of his fellow members, as well.

Each member should cooperate with the legal profession by supplying appropriate reports, opinions, and testimony concerning his patients' health; provided they have been properly and ethically requested.

VI. Each new member should cooperate fully with the clergy in carrying out their joint role in the care of people who have become patients; and should become familiar with the effects of various religious beliefs upon the practice of medicine.

VII. Each new member should thoughtfully recognize the vital role he individually plays in reflecting the public relations image of the medical profession.

His own personal conduct with patients, the lay public, and other physicians will eventually influence, in greater measure than perhaps he now realizes, how well or how poorly the community will judge the merits of all of us who have joined together in organized medicine.

Respectfully submitted,
William L. West, M.D., *Clerk*

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NEW BOOKS RECEIVED

Books received for review are acknowledged in this department and such acknowledgement must be regarded as a sufficient return for the courtesy of the sender. Selection will be made for review in the interests of our readers and as space permits. Books are listed with advance data supplied by publishers. Prices quoted are not guaranteed. For further information, address queries to the publishers.

Medical Laboratory Technology And Clinical Pathology. 2nd Edition. Edited by Matthew J. Lynch et al. W. B. Saunders Company, Philadelphia, 1969. 1359 pp. with 590 illustrations. $23.00.

Atlas Of Nuclear Medicine, Volume I: Brain. Edited by Frank H. DeLand, M.D. and Henry N. Wagner, Jr., M.D. W. B. Saunders Company, Philadelphia, 1969. 217 pp. with 383 illustrations on 112 figures. (13 in full color). $18.00.

A Controlled Clinical Trial Of A Diet High In Unsaturated Fat. American Heart Association Monograph Number 25. Edited by Seymour Dayton, M.D., Morton Lee Pearce, M.D. Sam Hashimoto, M.S., Wilfrid J. Dixon, Ph.D. and Uwamie Tomiyasu, M.D. The American Heart Association, Inc., New York, 1969. 63 pp. $4.00.

The Myocardium In Hyperfunction, Hypertrophy And Heart Failure. American Heart Association Monograph Number 26. Edited by Felix Z. Meerson, M.D. The American Heart Association, Inc., New York, 1969. 163 pp. $4.00.

A Synopsis Of Contemporary Psychiatry. 4th Edition. Edited by George A. Ulett, M.D. and D. Wells Goodrich, M.D. The C. V. Mosby Company, Saint Louis, 1969. 340 pp. $9.50.

Symposium On Renal Transplantation. Archives of Internal Medicine Symposia, Volume 2. Guest Editor: Roscoe R. Robinson, M.D. American Medical Association, 1969. 567 pp. $1.00.

Manual on artificial organs, Volume I. The artificial Kidney. A guide to understanding for the physician and for the patient. Yukihiko Nosé, M.D., Ph.D. Head, Artificial Organs Research Laboratory, Research Division; Staff, the Cleveland Clinic Foundation, Cleveland, Ohio. The C. V. Mosby Co., St. Louis, 1969. 343 pp. With 401 illustrations. $27.75.

Textbook of Pediatrics. 9th Edition. Edited by Waldo E. Nelson, M.D., Victor C. Vaughan, III, M.D. and R. James McKay, M.D. W. B. Saunders Company, Philadelphia and London, 1969. 1590 pp. with 527 illustrations. $21.50.

Atlas of Obstetric Technic. Second edition. Edited by J. Robert Wilson, M.D. The C. V. Mosby Company, St. Louis, 1969. 313 pp. with 58 plates including 375 illustrations by Daisy Stilwell. $19.75.

Circulatory and Respiratory Mass Transport. A Ciba Foundation Symposium. Edited by G. E. W. Wolstenholme and Julie Knight. Little, Brown and Company, Boston, 1969. 310 pp. with 101 illustrations. $12.50.

Bacterial Episomes and Plasmids. A Ciba Foundation Symposium. Edited by G. E. W. Wolstenholme and Maeve O'Connor. Little, Brown and Company, Boston, 1969. 268 pp. with 27 illustrations. $12.50.

Studies In Clinical Enzymology. Edited by D. P. Mullan. The C. V. Mosby Company, St. Louis, 1969. 238 pp. $12.00.

Cardiac Arrest and Resuscitation. Third edition. Edited by Hugh E. Stephenson, Jr., A.B., B.S., M.D., F.A.C.S. Professor of Surgery, University of Missouri School of Medicine, Columbia, Mo. The C. V. Mosby Company, St. Louis, 1969. 659 pp. with 223 illustrations. $29.50.

Duncan's Diseases of Metabolism. Sixth edition, Endocrinology and Nutrition. Genetics and Metabolism. Edited by Philip K. Bondy, M.D., C.N.H. Long Professor of Medicine, Yale University School of Medicine. In association with Leon E. Rosenberg, M.D., Associate Professor of Medicine and Pediatrics, Yale University School of Medicine. W. B.

Saunders Company, Philadelphia, Pa. 19105. Oct. 1969. 1413 pp, 330 illus. vol. 1.; 710 pp, 264 illus., vol. 2 $39.00, if purchased singly: $21.00 each.

Fundamentals of Inhalation Therapy. Donald F. Egan, M.D., Director, Section of Chest Diseases, New Britain General Hospital, New Britain, Connecticut; formerly Director, Department and School of Inhalation Therapy, Yale-New Haven Hospital, New Haven, Connecticut; Associate Clinical Professor of Medicine, Yale University School of Medicine, New Haven, Connecticut. The C. V. Mosby Co.. St. Louis, Missouri. With 148 illustrations. 468 pp. $11.00.

Mass Field Trials of The Diet-Heart Question: Their Significance, Timeliness, Feasibility and Applicability. Edward H. Ahrens, Jr., Panel Chairman of the Diet-Heart Review Panel of the National Heart Institute. The American Heart Association, New York, N.Y. 10010. 51 pp. $4.00.

Manic Depressive Illness. George Winokur, A. B., M.D., Professor of Psychiatry, Washington University School of Medicine, St. Louis, Missouri. Paula J. Clayton, B.S., M.D., Assistant Professor of Psychiatry, Washington University School of Medicine, St. Louis, Missouri. Theodore Reich, B.Sc., M.D., C.M., Washington University School of Medicine, St. Louis, Missouri; presently, Van Amerigen Fellow of the Foundations' Fund for Research in Psychiatry in Population Genetics at the University of Edinburgh, Scotland. The C. V. Mosby Co., St. Louis, 1969. 161 pp. $6.50.

NEW BOOKS IN REVIEW

DIAGNOSTIC ELECTROCARDIOGRAPHY. Edited by Michael C. Ritota, M.D. J. B. Lippincott Company, Philadelphia and Toronto, 1969. 174 pp. 227 figures. $15.00.

Reviewed by: LOUIS H. NAHUM

The author states that "the purpose of this book is to present simply and accurately the basic knowledge essential to the interpretation of the commonly seen electrocardiogram." It consists of diagrams drawn by the author and actual ECG's to illustrate each point discussed and every feature of the ECG of diagnostic value.

Each type of ECG is first presented diagrammatically and much enlarged for ease of visualization of the features characteristic of that type. The text calls attention to features of diagnostic significance and also to associated conditions. The normal cycle and its compounds P-Q-R-S-T-U waves are stressed in earlier chapters; the abnormal patterns are shown in the later chapters.

There are at least three different types of books on electrocardiography. In one the depolarization and repolarization currents are shown in a single myocardial cell. Then the patterns of electrocardiogram follow. Another type is that which attempts to analyze the idealized vectors of each portion of the electrocardiograms as drawn on a triaxial system. The third type is this book which gives patterns that when memorized can be used to interpret their clinical meaning. There is nothing new in this book, and this reviewer has corrected over a dozen statements with which he disagrees. There is no discussion at all of AV dissociation, the Wenckebach phenomenon parasystole, mimics of ventricular tachycardia such as W.P.W. PAT with aberrant I-V conduction and the Ashman phenomenon. There are no examples of RBBB and left anterior hemiblock. No inclusion of sinus arrest or SA block or AV dissociation as digitalis toxicity rhythms.

It is hard to know for whom this book should be recommended. Perhaps nurses and other paramedical personnel. The drawings are nice and the pictures are clear.

PRINCIPLES OF APPLIED BIOMEDICAL INSTRUMENTATION. Edited by L. A. Geddes and L. E. Baker. John Wiley & Sons, Inc., New York, London and Sydney 1968. 479 pp. $13.50.

Reviewed by: LOUIS H. NAHUM

This is a book that describes the basic principles by which physiological events are measured and each chapter is richly supplied with examples of the application of the principles discussed. In a carefully prepared index the reader, if he is problem oriented, can find information on all the methods that have been used to measure a particular event.

The authors however have rightly found from experience as have others as well that the emphasis of principles rather than the description of specific problems can spark ideas leading to unique and surprising solutions to new problems as well as in improvement of established techniques. Besides this, principles endure while methods themselves change with the passage of time.

The book actually brings together the fields of physiology and engineering in the effort to analyze problems in experimental physiology and medicine. It has done this both technically and historically. Because the qualified specialist is pressed for time he needs a book like this to familiarize himself with techniques and principles from other fields that might have genuine value to him in his work. Otherwise work could be duplicated by investigators who are unaware that the same problems may have already been successfully solved by men in other fields.

In essence the topics covered in this book are presented in "state-of-the-art" expositions in which the emphasis is placed on defining the parameters of the problems discussed. There is an extensive bibliography which each investigator should turn to, to investigate the original material in detail and by so doing to evaluate quickly the originality of his own ideas on a given subject.

The book is dedicated to Professor Hebbel E. Hoff formerly of Yale, scientist, scholar, teacher and physician to which should be added medical historian as well.

TEXTBOOK OF PEDIATRICS. 9th Edition. Edited by Waldo E. Nelson, M.D., Victor C. Vaughan III, M.D. and R. James McKay, M.D. W. B. Saunders Co., Philadelphia, London, Toronto, 1969. 1589 pp. $21.50.

Reviewed by: VICTOR L. SZANTON

This is quite a book. It took three editors to corral the works of 81 authors to put it together. Assembling these scripts into a well tempered text with an inviting table of contents is not easy. Pediatric practice is a conglomerate: the neonate, the infant, the preschooler and the adolescent, different creatures to be sure, but together all of a lump. Equating and paralleling chapter headings in the traditional format naturally is not possible. Roughly the book falls into three parts—the first covering the general field of pediatrics, development, nutrition and through a succession of headings, to the inborn errors of metabolism and then immunology and allergy. The second part has anatomic-physiologic systems, digestive, respiratory, cardiovascular, etcetera. The final section is a miscellaneous group of subjects; neoplasms, radiation injury, poisoning. This ninth edition is well organized, the index is thorough and carefully done and phenomenally helpful.

This text won't assist you much with the baby who is teething and raising hob with its family, it won't tell you much about what to do with a pesky, stubborn diaper rash or the baby who won't sleep at night—but it is a pediatric encyclopedia in scope. It will give you the high lights on important diseases, the chronic ones, the critical and dangerous ones—the rare ones. It has a good list of syndromes at the tail end of the book and all the latest on the inborn errors of metabolism. Rare as these conditions are, they are very much in vogue at this time. Even though you don't see them often, recognizing them can give you the comfortable feeling of being in the know, and the gratification of helping a sick child. For the young physician there is nothing he needs so much as this.

Do not use this volume for bedtime reading! You ought to have far better things than that to do. Besides, its weight, 1589 pages, will give you a pain in the manubrium.

If you are cramming for your pediatric boards, this is your best bet. Know this book! In that case get up at 4:00 A.M. After all, isn't that the best time to do your sharp reading?

CARDIOVASCULAR SURGERY 1968. American Heart Association Monograph No. 24. Edited by C. Frederick Kittle, M.D. The American Heart Association, Inc., New York, 1969. 274 pp. $4.00.

Reviewed by: GRAEME L. HAMMOND

Cardiovascular Surgery 1968 is a selection of 40 papers by Dr. Frederick Kittle from the 61 papers presented at the Cardiovascular Surgical session of the American Heart Association's 1968 Meeting. These papers primarily cover advances in five subjects: cardiac transplantation, coronary artery surgery, homograft valve replacement, prosthetic valve replacement, and surgery for congenital heart disease.

Cardiac transplantation is a particular field of interest but clearly remains in the germinal stage. Cooley reported a series of fifteen patients who underwent cardiac transplant. The six month mortality rate was 67% which is quite high even though all matches were of the C and D type. The great majority of these patients underwent transplantation for severe coronary artery disease (for which there now appears to be better and safer operations on the horizon). A paper on the physiology of the transplanted heart indicates that it functions adequately but not as efficiently as the original heart. The principal problem is rejection and there has been little progress on this front although there was an interesting paper on anti-lymphocyte serum.

There has been much work in the area of homograft valve replacements. Shumway reported 31 patients who underwent heterotopic living aortic homograft replacement for mitral valve disease with a 23% mortality rate and a zero incidence of valve emboli. The mortality rate included the early operations and this understandably would be reduced with experience. Unfortunately, however, significant problems remain in procurement, valve quality and infection. In regards to homograft replacement of the aortic valve, Malm reports that 44% developed aortic insufficiency although most of these cases were not serous. In this series, there was an operative mortality of 13.4%, which is about twice the mortality rate for prosthetic valve replacement. This is potentially one of the biggest fields for development and the book contains two interesting papers on the pathological changes which occur in homografts and a method of sterilizing the valve with electron beam energy.

The newer, totally cloth-covered prosthetic valves, while apparently decreasing the incidence of late postoperative emboli, have been shown to produce significant gradients across the valve due to tissue ingrowth. In Starr's series of 22 patients, there was a mean average gradient of 41 mm. Hg. across the aortic valve prosthesis and a 9.4 mm. Hg. gradient across the mitral valve prosthesis. The disc valves used in the mitral area, while decreasing aortic outflow obstruction, have also proved to have many complications such as substantial trans-valvular gradients particularly with exercise, disc grooving from contact with valve struts, and problems of disc cocking in an incompetent position.

Coronary artery surgery is in a stage of continuous and rapid growth. Direct coronary reconstructive procedures seem to be gaining slowly on the internal mammary artery implant as the procedure of choice in the treatment of this difficult disease. Of the several direct procedures available, saphenous vein bypass graft from the ascending aorta to the coronary artery distal to the point of obstruction appears to be the most promising. In Effler's series of saphenous vein grafts to the right coronary artery angina was completely and immediately relieved in all cases. The operation is associated with a 5% mortality rate which is quite respectable for this type of surgery. Investigation of internal mammary artery implant physiology continues and two papers explored the effect of myocardial tunneling on left ventricular function. Methods to determine areas of myocardial ischemia by electrocardiography on the operating table were presented and an interesting method to provide left ventricular assist was evaluated in calves.

Congential cardiac surgery remains on a plateau of excellence but a field of no startling advances. Waldhausen restates the importance of prolonged pulmonary ventilation after correction of ventricular septal defects associated with pulmonary hypertension and McGoon has tabulated the incidence of emboli from patches of atrial septal defect repairs. In McGoon's series of 546 patients, 35 developed emboli, 30% of which were fatal. Emboli occurred primarily in the older patient and he concludes that all patients over 40 in atrial fibrillation should be maintained on permanent anticoagulants after atrial septal defect repair.

Many horizons are open in cardiac surgery as this report indicates. The particular fields of interest and drive are the development of newer and better valve design, safer, more applicable operations for the treatment of coronary artery disease, and improved methods for circulatory assist. The American Heart Association and Dr. Kittle have done an excellent job in bringing together the advances in cardiovascular surgery which have taken place in the United States and Canada in the past year.

Hypertension In Children Still Unexplained

(*JAMA*, 210: 1846, December 8, 1969) Children, as well as adults, seem to be subject to unexplained or "essential" hypertension, a group of investigators found in a study conducted recently at Washington University School of Medicine, St. Louis.

The group studied 40 hypertensive and 40 normal children ages 4 to 18. They measured plasma renin activity, aldosterone excretion, creatinine clearance, and plasma and urinary electrolytes in both groups.

Only eight hypertensive subjects had findings that might account for the hypertension, Sol Londe, M.D., said in reporting the results at the American Heart Association meeting in Dallas.

There were more overweight children in the hypertensive group—32 compared with 8 normotensives. Fifteen hypertensive children had a parent with hypertension, compared with five in the control group.

Although the study suggests that obesity may play a role in hypertension and that there may be familial susceptibility, the real cause of high blood pressure in most children remains unclear, the investigator summed up.—L.H.N.

Roentgenograms Reveal Urinary Tract Infections

(*JAMA*, 210: 807, November 3, 1969) Radiological evidence of ureteral ileus, vesicoureteral reflux, or nonobstructive hydronephrosis in children should alert physicians to the probability of urinary tract infection rather than obstruction or anomaly, says Charles E. Shopfner, M.D.

Speaking of physicians at the 70th annual meeting of the American Roentgen Ray Society, he maintained that these three radiological findings usually indicate a need for medical treatment rather than surgery.

"We used to think these roentgen findings were due to obstructions," he told Medical News in an interview. "Now we know that they are the primary effects of the infection itself."

Dr. Shopfner recently studied 231 children under the age of six months by intravenous pyelography and cystourethography. Sixty-nine of the babies had septicemia and the other 162 children served as controls.

He found that approximately one-third of the children with septicemia demonstrated at least one of the three radiological indicators or urinary tract infection. Most of the children showed all three effects but without any obstructions.—L.H.N.

Payment For Lab Services

At the July 1969 annual meeting of the American Medical Association, the House of Delegates adopted a resolution regarding unearned markups on work referred to clinical laboratories. The purpose of the resolution was to point out the impropriety of MD's engaging in such a practice.

The resolution reaffirmed previous rulings of the Judicial Council that the laboratory, not the attending MD, should bill and collect directly from the patient or third payor for services. Under circumstances where this is impractical, the attending physician should state on the bill he submits to the patient the name of the laboratory performing the service and the exact amount of the charge paid or to be paid by the MD to the laboratory.

While the attending physician is entitled to a fair compensation for the professional services he renders, the resolution cautioned the MD that he is not engaged in a commercial enterprise and that any markup, commission or profit on the services rendered by a clinical laboratory is, therefore, exploitation of the patient.

Improper Markup

E. G. Shelley, MD, Chairman of the AMA Judicial Council, emphasized this point because some physicians seem to have the impression they may not charge for collecting a specimen from a patient and forwarding the specimen to a laboratory for analysis.

He added, however, that it is improper for a physician to mark up a charge made by an outside laboratory and pass the *marked up* charge on to the patient. Dr. Shelley cited one bill directed to the Judicial Council's attention for "serology, $7.50; cholesterol, $7.50; alkaline phosphatase, $7.50; complete blood count, $12; sedimentation rate, $6; glucose, $5; urea, $7.50; uric acid, $7.50." A total of $60.50.

This battery of tests was done for a charge of $6 to the physician. This, he said, is an example of marking up fees and is an unethical practice.

In cases where the attending physician performs laboratory services for his own patients, he is advised to provide information on the bill to show where the services were performed. The MD should include an adequate description of the services provided and the charges made.—*Massachusetts Physician*—January 1970

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Index to Advertisers

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Classified Advertising — — — — — — — — — — — — 139

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Hartford County Med. Association, Hartford, Conn. — 115

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CONTENTS

editorials

A Look Into The Future Of Society—Developing A Science for Survival . . . 145
Multiphasic Screening In The Next Decade . . . 146
The Effects Of Physical Training In Coronary Heart Disease . 148
Ectopic Beats More Dangerous Than Others . . . 152
Medical Coverage In A Coronary Care Unit Of A Community Hospital . . . 153
Some Global Impacts Of Applied Microbiology . . . 155
The Effect Of Aspirin On Arterial Thrombosis . . . 159
Lithium Carbonate In Affective Disorders . . . 160
Control Of Viral Infections: The Chemical Approach . . . 161
Senescence And Errors In Protein Synthesis . . . 162
Untreated Ca-in-situ Of The Cervix . . . 163

scientific

Hypokalemic Metabolic Alkalosis Due To Carter's Little Pills, *Basilia Ramirez, M.D.* and *Norman J. Marieb, M.D.* . . . 169
Serum Antinuclear Antibodies In Rheumatoid Arthritis, *Grace D. Hughes, M.D.* and *Naomi F. Rothfield, M.D.* . 171
Reliability Of Diagnostic Tests In Patients With Carcinoma Of The Lung, *Charles E. Morhardt, M.D.* and *Ernest J. Montgomery, M.D.* . . . 177
Puncture Wounds In Surgical Gloves, *William C. Butterfield, M.D.* . . . 180

departments

The President's Page . . . 182
From The Executive Director's Office . . . 201
Physician's Placement Service . . . 208
Woman's Auxiliary . . . 212

miscellaneous

Program—178th Annual Meeting . . . 165
Artists Attention . . . 168
Medical Grand Rounds—Yale-New Haven Hospital, Diagnosis and Management of Hypoglycemia, *Philip Felig, M.D., Frederick Lee Sachs, M.D.* and *Lewis Landsberg, M.D., Editors, Pamela Brooten, Assistant Editor* . . . 185
X-Ray Of The Month, *Arnold B. Rilance, M.D.* . . . 193
Electrocardiogram Of The Month, *Hyman N. Chernoff, M.D.* 196
British National Health Services, *Ned Thomas* . . . 198
Around The State . . . 210

Obituary:

J. Whitfield Larrabee, M.D. . . . 213
Michael J. Conroy, M.D. . . . 214
In Memoriam . . . 214
Meetings . . . 216
New Books In Review . . . 217

Connecticut Medicine

editorials

A Look Into The Future Of Society—Developing A Science For Survival

In the past we have had science for intellectual pleasure, science for control of nature, science for war. But today the whole human experiment may hang on the question of how fast we now press the development of science for survival. Nothing less than the application of the full intelligence of our society is likely to be adequate. The problems will require the humane and constructive efforts of everyone involved. The goal should be to add to the quality of human life and the realization of the full potential of every human being. In a way then, correcting societal ills will fulfill the philosophy of medicine.

We will need large numbers of scientists for social research and development, full time interdisciplinary teams combining men of different specialties, natural scientists, doctors, engineers, teachers, lawyers and many other trained inventive minds, to create the "social inventions" that have a chance of being adopted soon enough and widely enough to be effective. Of course, mobilizing scientists may not be enough unless we understand what is wrong and what it is we want righted. This, of course, will depend upon what our ultimate philosophy is. Otherwise, there is no guarantee that these problems can be solved or even solved in time no matter what we do.

The new science and technology have made our problem immense and interrelated although technology did not create human conflicts and inequities. This arose from the philosophy of laissez-faire in which the worth of the individual did not receive its full understanding. However, technology made the problems so vast as to become unendurable.

There are presently few people outside the research community who have the basic knowledge necessary for radically new solutions, or who can engage in research to find the solution to a posed or felt problem. Scientific research and the development of groups in institutions dedicated to research and training of societal doctors may be the only effective mechanism by which new ideas and new experts will come into being, will view societal ills with the same objectivity as medical scientists view human ills.

Some of the problems such institutions and these experts will have to tackle are already identified. Some are of such magnitude as to compel almost immediate solution. If we view the percent of the problems in terms of the size of the population that might be met or affected, then the one on top of the list is the danger of large scale or total annihilation by nuclear escalation or by radiological chemical-biological warfare. This crisis will continue until we get a safer peace-keeping arrangement. The peace-keeping stabilization problem will either be solved or we will be dead.

Then there is the probability of the destruction of our whole biological-ecological balance in the United States by mismanagement and pollution. Then also others fear political catastrophe as a result of divisive social and structural problems. These must be solved. On a world scale famine and ecological catastrophe head the list for constructive solution.

ABOUT THE COVER

LEEUWENHOEK AND "LITTLE ANIMALS"

ANTONY van LEEUWENHOEK, draper of seventeenth-century Delft, Holland, in his spare time retired to his "closet" to observe the wonders of the microscopic world through tiny lenses he laboriously ground and mounted. He was first to report having seen "animalcules"—protozoa and bacteria—and to confirm by direct observation circulation of the blood. Though 200 years elapsed before practical application of his discoveries contributed to medicine, his work laid the foundation for modern medicine's tremendous century-long onslaught against diseases caused by bacteria and other microbiologic entities—a campaign which has resulted in saving millions of lives.

A lower level of crisis problems include those already upon us, administrative management of communities, cities, slums, participatory democracy and racial conflict. The problems of pollution and poverty or major failures in the economy or in law and justice could escalate to serious levels of tension if they are not solved. The seriousness of any one, depends on the number of people they actually affect and the average distress they cause. Then there are the transportation problems and neighborhood ugliness and violent crimes that depress the lives of tens of millions for short periods every day. These evils are not negligible and they are worth the efforts of enormous numbers of people to cure them and keep them cured. On the other hand they will not destroy our society.

Probably no human institution will continue unchanged by the year 2000 because they will all be changed by the crises if they are not changed in advance to prevent them. There will surely be widespread rearrangements in all our ways of life every where from our patterns of society to our whole philosophy of man. Will they be more humane or less? Will they come to resemble a diverse and open humanist democracy or Orwell's 1984; or a past nuclear desert with its scientists gone? It is our acts of committence and leadership in the next few months and years that will decide. No society really wills a solution. But how can a solution be found anywhere until it is willed.

Since societal causes will not require secrecy, scientists from all over the world would have important thoughts to contribute. The real step that will probably be required in a short time is the creation of whole new centers where interdisciplinary groups can be assembled to work full-time on solutions to the crises problems. Such centers will include research development training of experts out of which will come new socio-technical conventions and a new breed of doctor, the Doctor of Society. We already have the counterpart in medical institutions where scientists with wide ranging interests in human biology work toward the solution of medical problems and the training of medical experts.

Even though we have had many social inventions adopted, the question remains why it is that in spite of these inventions, the world has gotten worse. Is it possible then to create social inventions that can solve our present crisis problems in order to make the world better? How do we make peace-keeping mechanisms? Why have they failed thus far? How do we increase our food supply to feed those we already have? How do we replace our present sterile and dangerous confrontations? Are there psychological and social theories that we can employ towards improvement in the quality of human life?

There will, of course, be need for money and power to overcome organizational difficulties and vested interests. If, however, we can point to future increase in human satisfaction, men will be willing to pay for it. A new world with blocks and malfunctions removed would be fantastically wealthy. Can we devise systematic ways for intelligence to convert our present difficulties into profitable solutions of our present problems? The answer is yes but we must commit ourselves to a search for the solutions. Who will begin to create institutions necessary to train the doctors of society to engage in research into causes and cures of societal ills. The time is terribly short.

L.H.N.

Multiphasic Screening In The Next Decade

Screening is a way of combating disease because its aim is to discover people who although they appear well are in fact suffering from some preclinical disease. By detecting disease in its early stages, the patient can then be given treatment before the disease takes a firm hold. If the discovered disease is familial or communicable, steps can be taken to prevent the spread of the disease.

Only a few centers equipped to perform comprehensive screening examinations are presently in operation. For example the Permanente Group in Oakland and San Francisco provides multiphasic health check-ups for plan subscribers. The Kaiser Foundation hospitals and Permanente Medical Group through a system of 9 hospitals and 19 clinics provide a comprehensive medical care program to 760,000 health plan members in the San Francisco bay area.

Tests in this screening procedure include medical history, analysis of blood and urine constituents, electrocardiography, mammography, Papanicolaou cervical smear, spirometry, audiometry, tonometry and much else. The data for all parts of the examination except cardiology, radiology and retinology are fed into a computer, analyzed and returned in a preliminary report to the pa-

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tients leaving the clinic. The computer checks for completeness, realistic values, "normal" ranges for age and sex and cross checks on other related information to determine whether they are consistent or contradictory.

When an abnormal response or combination of responses is obtained, the computer advises the performance of additional more specialized tests which are not part of the routine. Such screening centers are intended to provide an efficient means for the detection of abnormalities or indications of disease, but not to replace a full examination by a personal physician. Their purpose is to place in the hands of the examining physician a summary of basic data and to refer to the physician's care a person with indications of disease. The experience is that multiphasic screening does result in a reduction in much cost per test. Against this is, of course, the large number of tests many of which are unnecessary.

The technic has been criticized because in the past only test-positive patients were referred and the tests used were of poor quality. There has been a lack of real evidence that periodic examinations have a salutary effect on morbidity and mortality. Methods for bringing screening into the health-care system have been unavailable and scientifically based evaluation of the effectiveness of multiphasic screening and a long term benefit in relation to cost have not been available. However, multiphasic screening does allow for economics when large numbers are involved and it is probable that in the decade ahead, communities of 150,000 or more will have screening centers.

Unquestionably multiphasic screening has been undergoing rapid changes in concept as tests are becoming better instrumented, more quantitative and diagnostic. It is also likely that once the programs become widely available the practicing physician will more readily accept them. Nevertheless, the explicit role of multiphasic screening in health-care systems of the future remains a question. What is in the offing, however, is not hard to discern. Improved diagnostic instrumentation is on the way. Automated equipment to conserve the physician's time, improved instruments, devices and systems for modern automated clinical laboratories are being constructed. Improved data processing capabilities particularly input and output devices will be made. These future needs undoubtedly will stimulate industrial interests in producing the mechanical and electronic components needed for such screening systems.

As we glimpse into the future, the medical profession is going to be called upon to assimilate the advances of modern technology. There is a precondition to the satisfactory introduction of sophisticated instrumentation into our health care systems which will require adequately prepared and trained manpower. The clinical pathologist must become acquainted with physical methods of data handling. The nurse must learn new forms of record keeping and interpretation of such records and must understand the new instrumentation. Last but not least will be the need for highly skilled technical staffs to be trained to install, operate and repair these often complicated systems.

As the field of bioinstrumentation expands and bioinstrumentation technologists will have to be trained in increasing numbers, we may look forward to new centers where research teaching and engineering can be done on instruments for medicine and where scientists and technicians learn to use them.

L.H.N.

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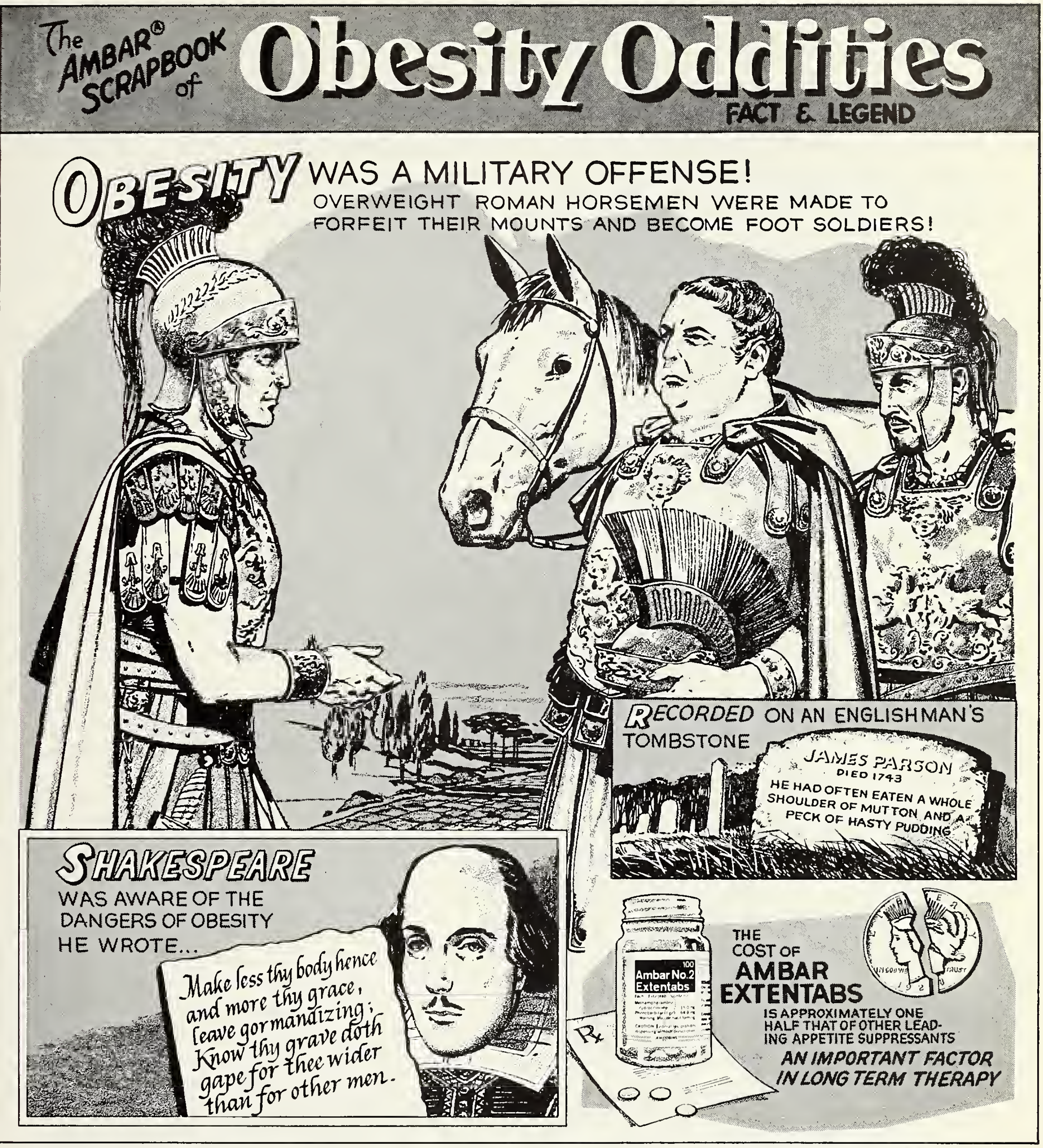
The Effects Of Physical Training In Coronary Heart Patients

The idea that patients with angina pectoris can improve by physical conditioning is an old one. Heberden[1] in 1772 described a patient who was nearly cured of his angina after sawing wood for six months. Twenty-seven years later, Parry[2] discussed the benefits of moderate physical exercise in patients with angina. Although this view was held by numerous distinguished physicians since then, the pendulum swung in the opposite direction, so that psychic heart cripples and the "Heart Scare Syndrome" developed from too much restriction of activity especially in the post myocardial infarction period. Recently there has developed an increased interest in the scientific evaluation of the effects of exercise on patients with coronary artery disease. For example, Gottheiner[3] in Israel reports on strenuous sports as treatment for degenerative heart disease. In this country investigations pointing to the benefits of exercise training programs were given early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BRIEF SUMMARY/**Indications:** Ambar suppresses appetite and helps offset emotional reactions to dieting. **Contraindications:** Hypersensitivity to barbiturates or sympathomimetics; patients with advanced renal or hepatic disease. **Precautions:** Administer with caution in the presence of cardiovascular disease or hypertension. **Side Effects:** Nervousness or excitement occasionally noted, but usually infrequent at recommended dosages. Slight drowsiness has been reported rarely. See package insert for further details.

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impetus by Hellerstein and his associates who reported their preliminary results in 1963.[4]

Why this improvement does occur is not yet fully understood. In fact this is due to absence of data which compares training responses in normal subjects of similar age to the coronary patient. Good data are available on young men and athletes, but these are not directly applicable to the problem of the coronary patient. If there were a successful animal model that mimicks closely human coronary heart disease, the subject could be solved. However, the circumstances of the dog whose coronary artery has been ligated experimentally are not necessarily relevant to clinical patients. Nevertheless, six years of application and research on the effects of physical training after myocardial infarction does offer some evidence about the mechanisms involved in the improvement seen following physical training.

Theoretically diminution of anginal symptoms during daily activity can occur as a result of decreased cardiac oxygen consumption, increased coronary blood supply or both mechanisms acting simultaneously.[5] If exercise caused more efficient muscle metabolism, then patients could perform their work with less oxygen requirement. This in turn would reduce cardiac work by reducing the need for peripheral blood flow to muscle and therefore reduce cardiac output and cardiac work. A counterpart to this concept is the view that nitroglycerin relieves angina pectoris by reducing the venous return and, therefore, cardiac output. In fact, the heart rate at a given work load has almost uniformly been found lower after short periods of training without affecting the aortic pressure. Such changes are similar to those of training responses in healthy young and middle aged men.

In the coronary patient, physical conditioning is not accomplished by increase in the ventricular diastolic volume. This is analogous to the response in middle aged men. Young men, however, develop increased diastolic volume in response to training. The increased diastolic volume is an important source of ventricular reserve for the Starling law proved that increased stretch of the myocardial fibre is followed by increased force of systolic discharge. Since both right and left ventricular function are improved after training in post-infarction patients, the increased force of ventricular systole in such patients must be derived from a factor other than the Starling principle. From animal experiments we know that this would lead to increased oxygen consumption.

There are, of course, other ways of improving cardiac efficiency in coronary patients by training without necessarily invoking increased oxygen consumption. One might be a more synchronous contractible pattern which would reduce oxygen demand by decreasing localized bulges. This would favorably alter the intramyocardial "stealing" of blood from well contracting to poorly contracting areas. An additional factor capable of reducing myocardial oxygen consumption would be a reduction of the sympathetic drive during exercise. Judging from the reduced heart rates on exertion in coronary patients after training, this probably takes place. We may say that the issue of efficiency is established.

But the crucial question is unanswered. Does a qualitative or quantitative change occur after training in coronary circulation via collaterals? From the large scale use of coronary angiography and former pathological studies by Schlesinger and Blumgart at Beth Israel in Boston, there is now ample evidence that collaterals do develop as a natural reparative process in coronary artery disease. The cause for the development of collaterals appears to be hypoxia for there is absence of collaterals in patients without angina and there is a high incidence of collaterals in patients with angina.[6]

The rationale of increasing the frequency of hypoxia stimulated by physical training is logical. However, objective evidence for increased collateral development after such a program is yet to be established. Recent studies in dogs with coronary ligation have failed to demonstrate any difference in the X-ray or post-mortem patterns of coronary arteries between trained and untrained animals.[7] Sporadic case reports in man have demonstrated collaterals but in one series of six, none showed enhanced collateral formation on repeated angiographic examination. It must be recalled, however, that coronary angiography is unable to detect changes in the smallest vessels. To demonstrate increased flow one would have to obtain measurements of coronary flow and changes in myocardial oxygen uptake. The disappearance or improvement of ischemia in the exercise electrocardiogram at a given heart rate is certainly suggestive.[8]

From the clinical point of view, physical training of post myocardial infarction patients seems to reduce anginal pain even though the mechan-

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ism behind this change needs more study. Furthermore, exercise renders the blood more fibrinolytic and since coronary artery disease patients seem to show increasing thrombotic tendencies, this is another good reason for physical training in coronary artery disease.

What we have learned from investigation on the effect of exercise in coronary patients is that training improves muscle efficiency, reduces their oxygen need for a given amount of work and, therefore, the work of the heart. It also improves myocardial efficiency, increases the development of collateral circulation in the heart and combats the thrombotic tendency so common in patients with coronary heart disease. What is now needed are studies on whether an increased life expectancy occurs in consequence of the physical conditioning in coronary disease subjects and whether such training will reduce the frequency of sudden death. This involves formidable clinical trials, but their potential for good is immense.

L.H.N.

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Ectopic Beats More Dangerous Than Others

Some ectopic beats are now recognized as more dangerous than others. This applies as well to the atrial as to the ventricular extrasystole. Smirk[1] noted that a group of patients with ventricular extrasystoles that were closely coupled to the preceding beat (R on T wave) had a high mortality because of ventricular fibrillation. Later, it was observed that the likelihood that an atrial premature beat could induce atrial fibrillation was directly related to the degree of its prematurity. It is this concept of myocardial vulnerability that can be applied to spontaneously occurring arrhythmia in man and by the aid of the electrocardiogram, some ectopic beats can be recognized as more dangerous than others.[2]

Sudden death has long been known to be a hazard of myocardial infarction (MI) and indeed of coronary heart disease in general. How frequent this complication is has been realized only recently. Several studies have now shown that the risk of sudden death is greatest in the first few hours after infarction before most patients have been admitted to the hospital.[3] Observations from CCU have revealed an extraordinarily high frequency of ventricular ectopic beats (VEB) in patients with acute infarction. Mortality can be decreased by a third to a half during hospitalization by prompt treatment for ventricular arrhythmia once it is recognized. The conclusion is inescapable that in some individuals VEB can be potentially lethal.

This being recognized, what should be done? Koch-Weser[4] reports on the effectiveness of prophylatic use of procainamide in preventing ventricular arrhythmia after acute MI. His study was carefully designed and controlled, using the double-blind technic, and ECG monitoring in patients uncomplicated by shock, heart block or severe heart failure. After a loading dose of 1 gram, the patients received either a placebo or 250-375 mg procainamide every three hours according to the patient's weight. Procaine afforded highly significant protection against all types of ventricular arrhythmias and markedly reduced the need for acute therapy of arrhythmias and prevented death from active arrhythmias. There were adverse effects encountered but only in those patients whose plasma concentration of the drug exceeded 6 mg per liter. Lower levels protected incompletely whereas concentrations of 7 mg per liter can produce adverse cardiovascular effects. Thus plasma procaine concentrations are helpful in establishing the proper individual dose.

Koch-Weser notes that previous studies of prophylactic anti-arrhythmia drugs have been unsatisfactory for a variety of reasons which include lack of proper controls and inadequate dosage of the drug in patients with MI. If one includes heart rate, then cardiac arrhythmias are common in patients with MI. They occur in as many as 95 percent. Ventricular tachycardia or ventricular fibrillation may occur in one third. Obviously to lower the mortality rate from acute MI, one must achieve prompt and effective pharmacologic or electric treatment of the serious arrhythmias. Thus the paper provides strong objective support for routine administration of an anti-arrhythmic drug in patients with MI.

Many problems, however, still remain. One is, which drug is best. Koch-Weser points out that procain has a short half-life and must be given every three hours with repetition of dosage by measurements of blood levels. We must remember, however, that the drug is not innocuous. One of the subjects may have died from toxic effects. Furthermore, we must bear in mind that procaine is currently the most common cause of drug induced lupus erythematous. Thus a truly satisfactory agent is not now available. What we need is a relatively non-toxic anti-arrhythmic drug with a prolonged action after infrequent oral administration.

What is more, the patients with MI are not the only group at risk for sudden death. Two separate studies[5,6] have shown that sudden death is 7-10 times more frequent in ambulatory men who have VEB detected during random ECG screening than in those who have not. Koch-Weser has shown that in a selected population prophylactic therapy works. The challenge then is to find a useful and effective anti-arrhythmic drug which is applicable both to the ambulatory as well as the hospitalized patient. We know that ectopic beats are common in the population at large. We must study our patients by the electrocardiogram as well to identify those for whom they are most dangerous.

L.H.N.

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Medical Coverage In A Coronary Care Unit Of A Community Hospital

It is now accepted that effective coronary-care units (CCU) have lowered mortality from acute myocardial infarction chiefly by reduction in deaths due to arrhythmias. In large medical centers with full time house staffs and unit directors, the units are covered twenty-four hours a day by both physicians and nurses trained for CCU duty. However, most of the 525,000 patients dying annually of myocardial infarction who do not die suddenly are managed in small community hospitals. If facilities in these hospitals are made available, they like those in the medical centers effectively utilized should also increase the salvage rate.

In a recent issue of the *New England Journal of Medicine* Church and Biern describe their plan for operating a CCU and the results they achieved over a three year period even though the hospital did not have a full time house staff. The significant fact emerges that these mortality figures are no worse than those achieved in medical centers. How did they accomplish this? Obviously, in the absence of full-time physicians, the responsibility for early recognition of serious complications as well as their management falls on the nursing staff. Accordingly all nurses were given a two-month training program consisting of lectures by staff physicians and supervised practical experience in the CCU. They are taught to recognize emergency arrhythmias and how to treat them. They gain experience in defibrillation by elective cardioversions performed under a physician's supervision. After a successful examination they were certified as qualified to perform special duties such as administration of emergency care including I.V. drug administration and electrical defibrillation if a physician is not immediately available.

Physician coverage is provided by a team of 8 physicians in private practice only two of whom have had special training in cardiology, but all trained in cardiac emergency care. Each member of the team takes charge of the unit for a three-day period during which he is on instant call. He regulates admissions, discharges and assumes responsibility for the treatment of all unit cases during his three days. He writes the admission note and orders in CCU. Although he carries out his private practice, during these three days of duty the CCU takes precedence and he must be immediately available. This assures prompt attention by a readily available physician thoroughly familiar with each case.

The personal physician records the admission history and physical examination. He follows his patient daily in the unit so that he is ready to take over when the patient is transferred out of the unit. He charges his patient his standard fee for hospital visits while the patient is in the unit while the CCU physician submits a consultation fee only for each new patient he admits, but not for other patients in the unit previously admitted.

Any patient with symptoms suggestive of acute MI may be accepted but priority is given to younger patients and those with most recent onset of symptoms and presence of arrhythmias. Intensive care begins immediately on arriving in the ER where there is a crash cart for immediate use. The patient remains in the unit for 5 days after onset of infarction or 3 days after control of serious arrhythmias. Ventricular tachycardia is treated aggressively with lidocaine. If pacing is needed in increasing A.V. block a pacemaker is inserted in radiology section. Patients with basilar rales are given only diuretics but receive digoxin if pulmonary congestion increases. Shock with symptoms of hypotension, peripheral vascular constriction, oliguria or mental changes are treated first by correction of rhythm disturbances and then metaraminol, norepinephrine, digoxin or isoproterenol depending on the patient's course.

In the 3 years 600 patients were admitted, 300 proved to have MI. In the CCU 39 patients died. The mortality rate was 7 per cent in "mild" cases, 31 per cent for severe and 9 out of 10 for shock. Unexpected ventricular fibrillation occurred in 30 patients and in 19 in absence of left ventricular failure 18 were successfully resuscitated and survived to leave the hospital. Since the management of serious arrhythmias is the main purpose of the CCU, these figures show how effective the CCU unit can function when physician and nurse are qualified to operate it.

The overall mortality compares favorably with experience of large medical centers. So are the mortality for unit patients and those admitted within 4-12 hours. The CCU appears to have influenced both the outcome of severe and shock cases. The physical design appears to be important, so that other patients in the unit are not disturbed, the patient's peace of mind is maintained as well as his confidence. Proximity of the nurse to the patient is important so she can be assisted in recognition of complications before she is alerted by the alarm.

In the absence of house staff or a full time physician, it is difficult for doctors in private practice to provide the intensive coverage that modern methods of coronary care require. Church and Biern's system of rotating responsibility among a team of qualified doctors insures the prompt availability of a trained physician. The training program arranged by Dr. Oscar Roth in which physicians become qualified in 2 weeks for taking charge of a CCU shows how quickly any interested physician can become competent in this area.

It appears that to give the duty physician during his three days responsibility for care that is total rather than limited to emergencies avoids the delay and misunderstandings that can result when semiurgent matters arise. Furthermore, control of admissions and discharges is simplified when one person is in charge of both care as well as assessing priorities.

To make such a system a success requires an atmosphere of trust and cooperation among the 8 CCU physicians, many of whom are in competition with one another in the private practice of medicine. Members of the community hospital staff who were not part of CCU team, have cooperated fully in this arrangement and after 3 years of experience no one has felt any need to change it. There is, of course, no reason why there could not be more than 8 physicians to rotate once they become competent.

This shows that a "closed staff" of competent physicians to provide optimal treatment in a CCU as recommended by Day[2] is certainly feasible in a community hospital. The scheme encourages physicians to make themselves qualified quickly. Moreover the patients have warmly accepted the system of multiple physician coverage.

L.H.N.

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Some Global Impacts Of Applied Microbiology

The third International Conference on Global Impacts of Applied Microbiology was held in Bombay from December 7-12, 1969, under the presidency of Dr. Vikram Sarahbac, Chairman of the Atomic Energy Commission of India. He stressed the interrelationship between microbiology and all branches of science. He cited an example of a project in Uttar Pradesh, where the government introduced into a rural area a vast amount of energy from atomic power. The chain reaction this started involved industrialization of a rural environment, change from agriculture to a predominantly industrial economy, urbanization, increasing water supplies, sanitation problems and control of environmental pollution.

Professor C. G. Heden of Sweden in his inaugural address, strongly advocated the abandonment of the microbiological warfare establishments run by the major powers and the deployment of the staff into peaceful purposes. He emphasized that these establishments for war preparation which will probably never be used, employed one of the major sections of the whole world's microbiologists of whom there is a great shortage. Nowhere else at present were there large scale facilities which could be turned to the production of pathogens to attack crop destroying insects and pests.

There is at present a tremendous amount of expertize and material "locked-up" in such establishments. Professor Heden cited as an example Pine Bluff Arsenal in Arkansas where 1700 persons were engaged in production and storage of chemical and biological smoke and incendiary materials. In 1966 the arsenal's area was 1500 acres and its buildings and equipment worth 138 million dollars. Average daily water consumption was equivalent to that of a town of 33,000 and its power consumption that of a town of 13,000 inhabitants.

The conference also devoted time to the problem of epidemiological surveillance. In the control of measles for example in Nigeria, the immunological status of the child population was such that measles innoculation was needed only up to age 5. In Togo it was needed up to age 7. In the control of enteric fever, J. Ungar reported that acetone treated vaccine was providing better protection than the more usual vaccines treated by heat, alcohol, or phenol. A study reported by H. A. Randhawa reported 8 percent of goat carcasses examined immediately after slaughter in Haryana were found to yield salmonella organisms, 38 percent pyogenic staphylococci and 22 percent hemolytic streptococci.

Professor Bloch reported sufficient evidence for use of BCG in developing countries against leprosy. BCG administration was now safer than small pox vaccine and could be given along with it. Lyophilized BCG vaccine could be transported under ordinary temperature conditions. He believed that in developing countries preliminary testing with tuberculin was superfluous.

The conference considered and noted with concern the increasing deterioration of the quality of fresh water resources throughout the world and recognized the need for new approaches to the treatment of water and waste water with emphasis on conservation and reusage. Microbiologists were urged to influence public opinion to this end.

Protein and Petroleum

A session which strongly stimulated the imagination was devoted to "single cell protein", i.e. protein produced by microbial agents. There is immense potentialities for the production of edible yeast proteins from petroleum which can be fermented by Candida tropicalis and other yeasts. Two pilot plants have been set up, one at Grangemouth by the British Petroleum Company and the other at Marseilles. It is estimated that the French output of yeast protein from petroleum will be 15,000 tons in 1970 and there are places for great expansion. Professor G. C. Senez of Marseilles stated that studies of the production of protein from petroleum were even more advanced in Britain.

Mr. C. A. Shacklady (British Petroleum Company) in a fascinating presentation first drew attention to the supreme importance of ensuring that protein from petroleum could be produced free from toxicity. Toxicity tests on this firm's products were almost complete and to date were entirely satisfactory. It is in animal foodstuffs that such protein is likely to have its greatest use and trials of it for pig and poultry feeding was described.

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IMPORTANT NOTE: INDOCIN (Indomethacin, MSD) cannot be considered a simple analgesic and should not be used in conditions other than those recommended under Indications. The drug should not be prescribed for children because safe conditions for use have not been established.

General Adverse Effects: Because of the high potency of the drug and the variability of its potential to cause adverse reactions, the following are strongly recommended: 1) the lowest possible effective dose for the individual patient should be prescribed. Increased dosage tends to increase adverse effects, particularly in doses over 150-200 mg/day, without corresponding clinical benefits; and 2) careful instructions to, and observations of, the individual patients are essential to the prevention of serious and irreversible, including fatal, adverse reactions, especially in the aging patient.

Indications: Symptomatic relief of adult rheumatoid and degenerative joint disease unresponsive to adequate trial of salicylates and other measures of established value, such as appropriate rest. Has been found effective in active stages of: 1) moderate to severe rheumatoid arthritis including acute flares of chronic disease, 2) moderate to severe rheumatoid (ankylosing) spondylitis, and 3) moderate to severe degenerative joint disease of the hip (osteoarthritis of the hip). Has been found effective in relieving pain and reducing fever, swelling, and tenderness in acute gouty arthritis in selected patients. May enable reduction of steroid dosage in patients receiving steroids for the more severe forms of rheumatoid arthritis; in such instances the steroid dosage should be reduced slowly and the patients followed very closely for any possible adverse effects.

Contraindications: Children 14 years of age and under; pregnant women and nursing mothers; active gastrointestinal lesions or history of recurrent gastrointestinal lesions; allergy to aspirin and indomethacin.

Warnings: *Gastrointestinal Effects:* Because of the occurrence and, at times, severity of gastrointestinal reactions, be continuously alert for any sign or symptom signaling a possible gastrointestinal reaction. The risks of continuing therapy with INDOCIN in the face of such symptoms must be weighed against the possible benefits to the individual patient. Gastrointestinal effects may be reduced by giving the drug immediately after meals, with food, or with antacids. Use greater care in aging patients.
Ocular Effects: Corneal deposits and retinal disturbances, including those of the macula, have been observed in some patients on prolonged therapy. Discontinue therapy if such changes are observed. Ophthalmologic examination at periodic intervals is desirable in patients on prolonged therapy.
Central Nervous System Effects: INDOCIN (Indomethacin, MSD) may aggravate psychiatric disturbances, epilepsy, and parkinsonism, and should be used with considerable caution in patients with these conditions. If severe CNS reactions develop, discontinue the drug.

Precautions: Blurred vision may be a significant symptom that warrants a thorough ophthalmologic examination. Patients should be cautioned about engaging in activities requiring mental alertness and motor coordination, as driving a car. Headache which persists despite dosage reduction requires complete cessation of the drug. May mask the usual signs and symptoms of infection; therefore, the physician must be continually on the alert for this and should use the drug with extra care in the presence of existing controlled infection. After the acute phase of the disease is under control, an attempt to reduce the daily dose should be made repeatedly until the patient is off entirely.

Adverse Reactions: *Gastrointestinal Reactions:* Single or multiple ulcerations of the esophagus, stomach, duodenum, or small intestine, including perforation and hemorrhage, with fatalities in some instances; gastrointestinal bleeding without obvious ulcer formation; perforation of preexisting sigmoid lesions (diverticulum, carcinoma, etc.); rarely, increased abdominal pain in ulcerative colitis patients or development of ulcerative colitis and regional ileitis; gastritis, which may persist after the cessation of the drug; nausea, vomiting, anorexia, epigastric distress, abdominal pain, and diarrhea.
Eye Reactions: Corneal deposits and retinal disturbances, including those of the macula, have been observed on prolonged therapy; blurring of vision.
Hepatic Reactions: Rarely, toxic hepatitis and jaundice, including some fatal cases.
Hematologic Reactions: Aplastic anemia, hemolytic anemia, bone marrow depression, agranulocytosis, leukopenia, and thrombocytopenic purpura. Since some patients manifest anemia secondary to obvious or occult gastrointestinal bleeding, appropriate blood determinations are recommended.
Hypersensitivity Reactions: Acute respiratory distress, including dyspnea and asthma; angiitis; pruritus; urticaria; angioedema; skin rashes.
Ear Reactions: Hearing disturbances, deafness, tinnitus.
Central Nervous System Reactions: Psychotic episodes, depersonalization, depression, coma, convulsions, peripheral neuropathy, drowsiness, mental confusion, lightheadedness, dizziness, headache.
Cardiovascular-Renal Reactions: Edema, elevation of blood pressure, hematuria.
Dermatologic Reactions: Loss of hair, erythema nodosum.
Miscellaneous: Rarely, vaginal bleeding, hyperglycemia, glycosuria, ulcerative stomatitis, and epistaxis.

Supplied: Capsules containing 25 mg indomethacin each, in bottles of 100 and 1000; capsules containing 50 mg indomethacin each, in bottles of 100.

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The pork, ham, chicken and eggs resulting had been submitted to a large panel of expert food testers who had been unable to distinguish between samples from control and petroleum protein-fed animals. It was estimated that from only 1 percent of the world's current consumption of mineral oil, 57 million tons of protein could be produced, enough to supply the whole world's needs for commercially produced animal food stuffs.

Here indeed is the birth of an industry based upon microbiology which could certainly have global impacts.

L.H.N.

Reference

1. Global Impact of Applied Microbiology, Brit. Med. J., I, 44 Jan. 3, 1970.

The Effect Of Aspirin On Arterial Thrombosis

During the 33 years since anticoagulation was first used on man, work to improve their quality, perfect their use and evaluate their therapeutic worth has been constant, productive, and even controversial. As far as treatment of the red thrombus (venous) there is little doubt about usefulness of Heparin and the coumarins in prophylaxis and therapy of thromboembolism. The major problem remains the platelet thrombus which occludes arteries and causes by far the greater morbidity and mortality. The importance of atherothrombosis is such that any agent which could prevent the platelet thrombus or cause its quick disintegration could favorably affect the outcome in many cases of coronary thrombosis and arterial thrombosis in the periphery. The field is far from static, however, and new agents are under development, study and evaluation.

Any substance which reduces platelet adhesiveness should theoretically have therapeutic value in arterial thrombosis for the arterial thrombus is a platelet clot aggregate which adheres to an atheromatous plaque. The platelets are said to adhere to an exposed collagen area of the plaque and by liberating adenosine diphosphate which renders the platelets more adhesive. One recent substance which is thought to prevent just this is aspirin.

Patients taking large doses of aspirin tend to bleed more easily than comparable controls. Quick[1] demonstrated a small but significant prolongation of bleeding time in normal subjects after they ingested 650 mg of aspirin and these findings have been confirmed by Weiss and Aledort.[2] In patients with bleeding tendencies secondary to coagulation disorders, the hemorrhagic effect is enhanced if they are given aspirin. O'Brien[3] has reported that the platelets may remain abnormal for many days after one dose of 300 mg of aspirin. The mechanism that inhibits aggregation of the platelets is not clear. Some evidence seems to point to action on platelet factor 3 with diminution of adenosine diphosphate release and of ATP.

Antithrombotic effects of aspirin have been reported in experimental animals; in rabbits with reduction of the incidence of thrombosis in extra corporeal shunts as well as an inhibition of the generalized Schwartzman reactions. In animals, aspirin appears to block thrombotic deposits on protheses and prolongs platelet survival. These effects appear to be due to acetylating certain sites in or on platelets. Al-Mondhiry, Marcus and Spaet[4] performed subcellular fractionation of labelled platelets and found that the labeled acetyl group was present in membranes, cytoplasmic granules and soluble fractions. Binding to the membranes is firm and probably irreversible. This is what may explain the sustained inhibiting effect of aspirin in platelet adhesiveness.

Similar inhibition has been reported by phenylbutazone and more recently some other drugs[5] but not with sodium salicylate. Apparently it is the acetyl radical which is essential to the effect of aspirin on platelet thrombi. Since aspirin is a relatively safe drug and phenylbutazone also especially if given for a short period of 4 days, this type of therapy in arterial thrombosis could well be undertaken even before the planned clinical studies will be reported of the effect of these drugs which are being undertaken in the United States and Great Britain.

The indications for clinical use aside from arterial thrombosis are not clear. Even in acute coronary occlusion we must remember that almost half are due not to a thrombus occluding the lumen but a subintimal hemorrhage. Obviously even if the antithrombotic drugs are found useful, at best they could change the outcome only in about half of the patients with obstructed arteries.

The next few years should bring a critical evaluation of the usefulness of these drugs for their new therapeutic application. The new planned studies with acetyl salicylic acid and phenylbutazone and other agents affecting the aggregation and activity of platelets are certainly of sufficient interest to warrant intensive exploration in this field.[6]

L.H.N.

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Lithium Carbonate In Affective Disorders

Lithium salts have been used successfully in over 1,000 cases of acute mania. Lithium compounds have also been reported to be effective when used prophylactically against recurrent mania and depression. Even in acute depression uncontrolled clinical trials have reported lithium salts to be effective. There, however, remains considerable controversy and skepticism surrounding this drug probably because of the low ratio of controlled to uncontrolled studies.

A recent controlled study by Goodwin and associates[1] should help to bring some clarification into this controversy. They studied 12 manic and 18 depressed patients longitudinally at the National Institute of Health. Double-blind ratings of mania and depression were recorded on a daily basis by a psychiatrist and trained nursing research team. The design involved an initial placebo period, a period with lithium carbonate, and then one or more placebo periods, allowing for direct comparison of drug and placebo periods within each patient.

They used strict criteria; consistent improvement with lithium carbonate coupled with consistent relapse on placebo. They were able to demonstrate that some improvement occurred in 40 percent of the depressed patients about half of whom showed a complete response. Three quarters of the manic patients responded. In addition the majority of the manic patients showed within 24 hours a rapid onset of relapse following placebo substitution.

The study is directed to some important issues both in psychopharmacological research as well as phychobiologic ones. The method of longitudinal evaluation in which several drug and placebo periods are compared within the same patient by use of double-blind ratings, clearly offers some distinct advantages, particularly in allowing one to draw solid conclusions from a smaller number of patients.

The question of lithium effects in depression is currently the focus of much controversy. The results of Goodwin's investigations are particularly illuminating in this area. Other controlled studies of lithium in depression reported only a weak anti-depressive effect.[2] It appears, however, that differences in patient selection might be the causes of the controversy. Goodwin found their positive results essentially only in those depressed patients with manic-depressive histories. Accordingly they are careful not to recommend lithium carbonate as an anti-depressant. Furthermore, they take the position that at this point their results in depression are primarily of theoretical interest.

However, the possibility that the same drug has a therapeutic effect on the "opposite" state of both mania and depression raises some important questions concerning the biological substratum of these pathological mood states. Lithium has been shown to affect both electrolyte and biogenic amine metabolism. These are the substances around which are focused the two major hypotheses concerning the biology of affective illness.

In mania there has been a scarcity of adequate agents until lithium was introduced. It can, therefore, serve as an important clinical tool. It can provide the basis for both pharmacological and biological investigation of affective illness.

The possibility of the drug being useful in some cases of acute depression is an important one as is its potential as a prophylactic agent to prevent mania.

L.H.N.

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2. Fieve, R. R., Platman, S. R., The Use of Lithium in Affective Disorders: 1. Acute Endogeneous Depression, Amer J. Psychiat *125* 487 1968
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Control Of Viral Infections: The Chemical Approach

At present there are only three substances which may be considered of some clinical use. Thiosemicarbazone for prophylaxis for smallpox, Adamantanamine for prophylaxis of influenza and certain metabolic inhibitors for treating corneal infection with herpes simplex virus. Most recently RNA has been used by instillation in the conjunctiva for this infection. Vaccines and interferon are prophylactic and do little once the cell is infected. The present hope for the cure of viral infections in the individual cell seems to rest on the chemical approach and this fact has encouraged continued effort in viral chemotherapy.

Points for specific viral attack rest on the recognized events in viral infection in cells which are specific to the virus. The events include contact of the cell with the virus, cell penetration, decoating of viral nucleic acid, synthesis of viral nucleic acids and proteins (structural and enzymatic) and assembly and release of new virus particles. A principal goal in viral chemotherapy should be the ihibition of viral nucleic acid synthesis. This conceivably could be accomplished through the use of selective inhibition of viral nucleic acid synthesis which have no structural analogy with viral nucleic acids and which are not incorporated into them, or through the use of a structural analogue which are incorporated into the viral nucleic acids giving fraudulent and nonfunctional nucleic acids.

Alternatively inhibitors might be prepared which block the early proteins (polymerases) that are essential to the synthesis of viral nucleic acid. One kind of inhibitor to be sought would be one which prevents translation from viral but not from hostcell messenger RNA. Most important, such inhibitors ought not to be incorporated in the cells genetic material. Research in viral chemotherapy has not yet achieved the status of an exact science, so that random screening as well as rational approaches will probably be continued to be used. Certainly in this search studies will not be limited to substances that are nontoxic for cells. They may search for specific antiviral and intracellular activities of a number of substances which may lead to synthesis of nontoxic antiviral compounds on a more rational basis.

In Glasgow, Suback-Sharpe et al have tested the effect of the antibiotic rifampicin on the multiplication of thirteen different viruses. It seems to inhibit the multiplication of thirteen different viruses especially of the DNA type vaccinia, cowpox, and adenoviruses but has no effect on the multiplication of RNA viruses including polio and influenza. The toxic effects of the antibiotic on the host cell seems to be the result of contaminants in the groups sample which will have to be removed if the antibiotic were to be used clinically.

One should bear in mind also the fact that the purpose of viral chemotherapy is to treat disease and that this might be achieved in part through attack on aspects of viral infection other than the virus itself. It is becoming clear that all or part of the pathology in certain viral infections may be due to allergic hypersensitization and to other immune phenomena. This has been recognized in many examples such as deep stromal effects of sensitization in herpes simplex infection. It is also recognized in the role of immune phenomena in bringing about fatal disease in otherwise normal mice that had been rendered immunologically tolerant by congenital infection with lymphocytic choriomeningitis virus.

The development of any measure for the control of viral disease by whatever method is necessarily a slow painstaking process for which a sophisticated technology must be evolved and a large body of information accumulated. Many hurdles need to be overcome before the stage of routine manufacture of even a vaccine is reached. Overall achievement requires the cooperative team play of a variety of disciplines including at the very least the fields of virology, cell biology, biochemistry, biophysics, pathology, epidemiology, applied biology and clinical medicine.

With this teamwork and a fantastically large outlay of funds and facilities we have succeeded in eliminating smallpox and reduced polio and measles and soon rubella and mumps to all but negligible levels. It is difficult to predict the extent to which vaccines will eventually be used to control acute infectious diseases. This will surely be influenced by the extent of collateral developments of alternative measures in the use of chemotherapy and host resistance.

When we are well on the road to conquest of viral infections major attention will be directed to control of the illnesses of obscure etiology for which at present viruses are only suspect as causative agents. The myriad possibilities of viral effects on cells including genetic addition, genetic deletion, genetic rearrangement, neoplastic transformation, antigenic alteration, biochemical malfunctions, release of sequestered antigen, cell dilution and the like, lend some credence to the view that viruses may play a role in the vast majority of the illnesses of mankind.

We have as yet no idea as to the degree to which viral vaccines may prevent such illnesses. It does seem possible that widespread use of existing and yet to be developed vaccines may eliminate or reduce the future incidence of illness in which a viral role is not even suspect at present. "Such is the wave of the future."

L.H.N.

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1. Hillman, M. R.: Toward control of viral infections of man. Science, 164: 506, May 2, 1969.

2. Suback-Sharpe, J. H., Timbury, M. C. and Williams, J. F.: Rifampicin inhibits the growth of some mammalian viruses. Nature, 222: 341, 1969.

Senescence And Errors In Protein Synthesis

Some time ago a view was proposed that cells age because they develop chromosomal mutations. Cells like sperm can remain normal by throwing off the mutated cells in the course of reproduction. On the other hand cells in the body that no longer divide like muscle and brain can accumulate chromosal aberrations and in time this produces senescence. In line with such thinking L. Orgel suggested that the crucial molecular events that lead to senescence are the occurrence and accumulation of errors in certain classes of enzymes. This would appear to be a derivative of the chromosomal theory of aging.[1]

Orgel argued that mistakes during the synthesis of most proteins would be irrelevant to aging because the altered molecules would simply be deleted out in dividing cells. But if any enzymes involved in DNA synthesis or protein synthesis contained errors which change their specificity then the result may be to induce errors in the protein being synthesized. Once the protein synthesizing machinery of a cell is contaminated in this way errors would accumulate exponentially and the cell would be unable to rectify the fault which would be passed on through the cytoplasm to the daughter cells.

Then once a critical threshold was reached the cells would suffer an "error catastrophe" and die. A small body of evidence has accumulated since 1963 which is compatible with Orgel's hypothesis. Among these is Holliday's[2] latest series of experiments with two species of fungi which fulfill one of its predictions—that an increase of the frequency of errors during protein synthesis should accelerate aging. Two years ago Holliday reported that if he fed Drosophila larvae with analogs of amino acids or streptomycin it shortens the life span of adult flies which emerge. His explanation was that these techniques increase the frequency of mistakes during protein synthesis.

In his latest experiments with species of fungi, Holliday used the same basic approach as in those with Drosophila. He found a correlation of accelerated aging with increased frequency of mistakes in protein synthesis in fungi. One species Podospora aserina undergoes a very characteristic growth cycle. On a solid medium the fungi hyphae grow at a constant rate and then stop growing, swell up, become pigmented and finally burst and die. If he so manipulated the growth conditions as to encourage the induction of mistakes during protein synthesis, then the aging of Podospora hyphae is accelerated.

When Holliday used Neurospora crassa it permitted an even more critical test of the protein error hypothesis. Neurospora unlike Podospora, normally grow for very long periods without any apparent aging. Eventually it enters a stop-start cycle known to mycologists as the "stopper" stage. At present it is not known whether the cause of this irregular growth is the same as that of senescence of Podospora. However, certain mutants of Neurospora have been isolated with much the same pattern of growth as Podospora. One of these grows for a while at a constant rate and then quite suddenly stops growing and dies.

The question was whether the mutant strain which is called the natural death (nd) strain makes more errors during protein synthesis than the wild type. Holliday believes it does. The nd strain appears to have an adenine enzyme mutation which can be overcome by crossing with a strain that contributes the adenine enzyme.

The critical test now is to show that the cytoplasm of aged calls contains more abnormal proteins than the cytoplasm of young cells from the same species. In most organisms it has thus far not been possible to distinguish between nuclear and cytoplasmic degenerative changes during aging. With fungi, however, it is usually possible to distinguish between nuclear and cytoplasmic control of particular phenotypes.

The hypothesis about senescence then is that it is a result of breakdown in the maintenance and accuracy of protein synthesis. In Podospora premature senescence can be induced by treatments which may reduce the accuracy of amino acid incorporation.

L.H.N.

References

1. Inheritance of old age. Nature, 221: 1191, March 29, 1969.
2. Holliday, R.: Errors in clonal synthesis and clonal senescence in fungi. Nature, 221: 1224, March 29, 1969.

Untreated Ca-in-situ Of The Cervix

Attitudes towards in situ epidermoid carcinoma of the cervix in Connecticut vary widely among different surgeons and gynecologists. Most believe that this diagnosis should lead to performance of a prompt complete hysterectomy. A few are willing to be satisfied with simple conization and to follow the patient with "Pap" smears, particularly if the subject is young and desirous of having more children. A few surgeons take the viewpoint that "cancer is cancer" and proceed vigorously with radiotherapy or Wertheim procedures or both.

A recently reported study from Ohio State University School of Medicine[1] bears importantly on the subject. Doctors Old and Jones were able to investigate 23 patients with biopsy or conization of the cervix in whom the diagnosis of carcinoma in situ was not made at the time (1952-1956) but only on review of the slides in 1964-5 during a comprehensive restudy of over 3,000 cervical biopsies. The diagnoses were agreed on by a panel of pathologists. None of these patients received radiotherapy or underwent hysterectomy or other therapy. Here, then, was a group of 23 patients with long-standing epidermoid carcinoma-in-situ of the cervix whose only treatment was the original biopsy or conization. Many of the patients had been pregnant in the interim.

All 23 were followed in 1964 and 1965 and the present status of the cervical lesion determined. The results were as follows:

1. Only 1 patient showed invasive carcinoma (stage I). This appeared 8 years after the original conization and was Class I when discovered.
2. 3 (13%) had demonstrable residual carcinoma-in-situ and 1 had residual dysplasia.
3. 18 (78%) showed *no* residual carcinoma-in-situ clinically, by smear (15 cases) or by histological study (3 cases).

The authors conclude: "The low incidence of detectable residual in situ carcinoma and especially of invasive carcinoma, as well as the long temporal evolution of the lesion and late invasive transformation indicates that temporization without hysterectomy can be undertaken with safety in selected patients. The fact that the lesion may persist or redevelop and become invasive means, of course, that patients must be closely and regularly followed if a hysterectomy is not performed." This common-sense attitude seems thoroughly justified by the data they present. It provides no support for a "cancer is cancer" attitude applied to epidermoid carcinoma-in-situ of the cervix.

Roy N. Barnett, M.D.

References

1. Old, J. W. and Jones, D. G.: Squamous carcinoma in situ of the uterine cervix; III A long-term follow-up of 23 unsuspected cases of 6- to 10-year duration without interim treatment. Cancer 18, 1622-1630, Dec. 1965.

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Inositol	10 mg.
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Zinc (from Zinc Oxide)	0.25 mg.
Iodine (from Potassium Iodide)	0.25 mg.
Calcium (from Dicalcium Phosphate)	72.5 mg.
Phosphorus (from Dicalcium Phosphate)	55 mg.
Potassium (from Potassium Sulfate)	2.5 mg.
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Magnesium (from Magnesium Sulfate)	0.5 mg.

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ACTION AND USES—*DOSAGE:* 1 tablet after breakfast and supper, or as required. In females, 3-week courses of therapy are recommended followed by a 1-week rest period. Withdrawal bleeding may occur during the rest period. *PRECAUTIONS:* Administer cautiously to female patients who tend to develop excessive hair growth or other signs of masculinization. *CONTRAINDICATIONS:* Patients in whom estrogen or androgen therapy should not be used, as in carcinoma of the breast, genital tract, or prostate, and in patients with a familial tendency to these types of malignancy. *AVAILABLE:* Bottles of 30, 100, and 500 tablets. Rx only. Also available: Testand-B injection . . . vials of 10 cc.

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GERIATRIC

178th ANNUAL MEETING
CONNECTICUT STATE MEDICAL SOCIETY

Hartford Hilton Hotel
10 Ford Street, Hartford, Connecticut

May 12, 13, 14, 1970

PRELIMINARY PROGRAM

TUESDAY, MAY 12

ANNUAL MEETING OF THE HOUSE OF DELEGATES

TERRACE ROOM —:— MEZZANINE

Kenneth F. Brandon, Hartford, Conn., Speaker of the House, presiding
Frank K. Abbot, Waterbury, Conn., Vice-Speaker of the House

7:30 Registration of Delegates
Continental Breakfast for Delegates and Official Guests

8:30 Call to Order
Opening Session

11:45 Reference Committee Hearings—Cities Rooms—Mezzanine
Luncheon—Fourth Floor Rooms

4:00 Final Session—Terrace Room

6:30 Adjournment
Delegates' Reception and Dinner—Cities Rooms

ROUND TABLE DISCUSSIONS

Members of the Society are invited and encouraged to participate in the new learning technique which was initiated last year; Round Table Discussions, or "Learning Panels". Six of these panels will be held on Wednesday, May 13 and six on Thursday, May 14th. The subject, time and place for each is published in the Program that follows. The respective "Learning Panels" will be chaired by experienced physicians who will lead their groups, of not more than 15 participants, through in-dept examination of the topics assigned. Active participation in the group discussion will be limited to members who have pre-registered. (Registration Forms will be mailed to members with the Program of the meeting). Members who have not pre-registered will be welcome to attend the Panels as observers only, within the limits of available seating capacity.

WEDNESDAY, MAY 13

SCIENTIFIC PROGRAM

MORNING SESSIONS

8:30 Registration—Mezzanine

ROUND TABLE DISCUSSIONS

9:00-10:30 Fourth Floor in Rooms Designated

Some Pitfalls in Interpreting Electrocardiograms—Room 424
Group Leader: Edgar Lichstein, New Britain, Conn.

Diabetes Mellitus—A Re-examination—Part I—Room 420
Group Leader: Leonard Vinnick, Stamford, Conn.

Thyroid Physiology and Function Tests—Room 416
Group Leader: Gerard N. Burrow, New Haven, Conn.

Obesity—A Re-examination—Room 412
Group Leader: Philip Felig, New Haven, Conn.

Renal and Adrenal Causes of Hypertension—Room 408
Group Leader: Peter M. Shutkin, New Canaan, Conn.

New Tests for the Evaluation of Hypothalamic Pituitary and End, Organ Function—Room 404
Group Leader: Bruce F. Bower, Hartford, Conn.

10:30 Intermission to Visit Exhibits

TERRACE ROOM

Moderator: Seymour Reichlin, Newington, Conn.

11:00 New Concepts in the Role of the Hypo-Thalamus and the Control of Pituitary Function
Seymour Reichlin, Newington, Conn.

11:40 Diagnosis and Treatment of Pituitary Disorders With a Discussion of Cushing's Disease
David H. P. Streeten, Syracuse, New York

12:20 Discussion—Questions and Answers

12:30 Luncheon—Cities Rooms
Intermission to Visit Exhibits

WEDNESDAY, MAY 13

AFTERNOON SESSION

TERRACE ROOM

Presiding: William F. Eckhardt, Jr., New Canaan, Conn.

2:00 Disorders of Androgen Metabolism in the Female
C. Wayne Bardin, Bethesda, Maryland

2:40 Problems of the Disorders of Androgen Metabolism as it Refers to Clinical Problems of Hypogonadism
C. Alvin Paulsen, Seattle, Washington

3:20 Discussion—Questions and Answers

3:30 Section Meetings

EVENING PROGRAM

6:15 Reception—Mezzanine

7:00 Annual Dinner of the Society—Terrace Room

THURSDAY, MAY 14

SCIENTIFIC PROGRAM

MORNING SESSIONS

8:30 Registration—Mezzanine

ROUND TABLE DISCUSSIONS

9:00-10:30 Fourth Floor in Rooms Designated

Some Pitfalls in The Diagnosis of Cardiac Arrhythmias—Room 424
Arthur O. Phinney, Jr., Hartford, Conn.

Diabetes Mellitus—A Re-examination—Part II—Room 420
David S. Wilcox, Hartford, Conn.

Thyroid Nodules and Thyroid Carcinoma—Room 416
(A Medical versus a Surgical Approach)
Group Leaders: William F. Eckhardt, Jr., New Canaan, Conn.
Malcolm M. Ellison, New London, Conn.

Disorders of Calcium Metabolism—Room 412
Donald M. Kanter, Stamford, Conn.

Some Endocrine Aspects of Male and Female Infertility—Room 408
Jerome J. Klein, Norwalk, Conn.

Dermatological Aspects of Endocrine Disease—Room 404
Sidney N. Klaus, New Haven, Conn.

10:30 Intermission to Visit Exhibits

TERRACE ROOM

Presiding: Paul F. McAlenney, New Haven, Conn.

11:00 Disorders of Growth
Robert M. Blizzard, Baltimore, Maryland

12:30 Luncheon—Cities Rooms

Intermission to Visit Exhibits

THURSDAY, MAY 14

AFTERNOON SESSION

TERRACE ROOM

PROGRAM ARRANGED WITH CONNECTICUT SOCIETY OF AMERICAN BOARD SURGEONS

2:00 An Internist Looks at Endocrine Surgery
Alfred Segaloff, New Orleans, Louisiana

2:45 Recent Advances in Endocrine Surgery
David M. Hume, Richmond, Va.

3:30 Discussion—Questions and Answers

3:30 Section Meetings

Artists — Attention!

GENERAL INFORMATION: The Connecticut Physicians' Art Association is planning the 1970 Art Exhibit in conjunction with the annual meeting of the Connecticut State Medical Society. The following information is submitted for guidance to art hobbyists.

WHERE: Hartford Hilton Hotel, Hartford, Conn.

WHEN: May 12, 13, 14, 1970

ELIGIBILITY: Physicians (members of the Connecticut State Medical Society) and their families are cordially invited to join this group of art hobbyists. (In the case of children and other members of physician's family, kindly indicate relationship to sponsor.) All previous exhibitors are invited to show their works at this meeting, and new exhibitors are welcomed. Works eligible will include oil, water colors, tempora, black and white etchings, photography, pastels, collages, mixed media and sculpture. Paintings over 24 × 30 will be hung only at the discretion of the art committee depending upon available space.

JUDGING: Art works will be judged in four categories: 1. Children under 16 years (children over 16 will be judged with adults); 2. beginners; 3. intermediates; 4. professionals. Pictures should be framed and wired for hanging. The exhibit will be judged by professional artists.

COST: A hanging fee of two dollars ($2.00) will be charged for each entry and fifty cents (50¢) for children under 16 years with two entries per artist. (Space requirements have caused our limiting the entries to two this year, as just noted.)

HOW TO APPLY: Entry blanks will be mailed to former exhibitors and also may be obtained by writing to the addresses of the committee listed below. One half of the entry blank should be submitted to me at the below address with your check prior to April 20, 1970. The other half should be attached to the picture. Make checks payable to the Connecticut Physicians' Art Association. Please fill in entry blanks completely so that entry can be categorized early in the above noted four categories.

SUBMITTING: Art works must be submitted to a representative of the Art Association in the lobby of the Hartford Hilton Hotel on Sunday, May 10, between the hours of 12 and 3 P.M. Parking temporarily near the side entrance is possible for the few minutes involved in dropping off these art works. It may be possible to aid exhibitors with the transportation of art works by contacting members of the committee noted below. These art works must be picked up on Thursday, May 14, between 12 and 4 P.M. Members of the art committee or their representatives will be in attendance at the display throughout the exhibit at the state meeting. The Connecticut State Medical Society, the hotel (nor the Art Association) can assume no responsibility for loss or damage of any cause to art works.

Under no condition can art work be accepted after MAY 10th.

If further information is needed, the following persons may be contacted:

Eugene Rightmyer, M.D., President, 114 Sherman Ave., New Haven; Mrs. Orvan Hess, Vice President, 29 Old Orchard Road, North Haven; Ann Murphy, 8 E. Normandy Drive, West Hartford, Chairman, Art Committee, Women's Auxiliary, CSMS; Mrs. John Shoukimas, 26 Pheasant Hill Dr., West Hartford; Edward Williams, M.D., 580 Hillside Ave., Naugatuck; Herman Austrian, M.D., 935 White Plains Road, Trumbull; Kurt Oster, M.D., 880 Lafayette Blvd., Bridgeport; Stewart J. Petrie, M.D., 56 Minerva St., Derby; Mrs. Mark Hayes, 163 Ridgewood Ave., North Haven; Mrs. Henry Sherwood, Penfield Hill Rd., Portland; Mrs. Clifford Wilson, 19 East Town St., Norwich; Mrs. Lowell Olson, 85 River Rd., North Haven.

Eugene Rightmyer, M.D., *President*
Connecticut Physicians' Art Association

Hypokalemic Metabolic Alkalosis Due To Carter's Little Pills

Basilia Ramirez, M.D. and Norman J. Marieb, M.D.

Case Report

Abstract:

A case of hypokalemic metabolic alkalosis due to the clandestine ingestion of Cater's Little Pills® is described. Many serious disease states may be considered in the differential diagnosis of hypokalemia with alkalosis and unwarranted surgery may occur because of the colonic x-ray changes. The habitual intake of cathartics must be considered when a patient presents with unexplained hypokalemia.

A 35-year-old housewife was admitted to the hospital for evaluation of weakness, lower abdominal cramping, weight loss, and fascial pigmentation. At age 32 there was an abrupt cessation of menses not associated with delivery or drug ingestion. 18 months before this admission lower abdominal cramping began, reportedly not associated with diarrhea. At that time while she was receiving a short course of oral contraceptive medication to induce menstrual flow, a barium enema showed "thumbprinting" and smoothly narrowed areas of colon. At laparotomy the bowel appeared normal, and an appendectomy and wedge biopsy of the right ovary were performed. The appendix showed only melanin pigment deposition and the ovary revealed normal cortex with many primordial follicles. There was a gradual return of all preoperative symptoms soon after surgery. Progressive weakness, poor food intake, and a 20-lb. weight loss were noted three months before this admission. There was also an associated marked irritability and a questionable increase in fascial pigmentation. The patient denied being ill but at her family's insistence sought medical care. She denied drug ingestion of any kind, vomiting, diarrhea, nocturia, orthostatic symptoms, or salt craving.. Her initial description of bowel movements was one formed brown stool daily.

Physical examination revealed a quiet cachectic white female 62 inches tall, weight of 94-lbs., B.P. 98/60 both supine and standing. Pulse was 80/min. and regular. Her face was deeply pigmented especially in the malar area. The breasts were atrophic but the quantity and distribution of body hair was unremarkable. The thyroid gland was not enlarged. There was no bowel distention noted and bowel sounds were active. Deep tendon reflexes were equal and not depressed. Mild left adnexal pain was present on pelvic examination. A sigmoidoscopy showed pale mucosa with no melanin pigment.

Laboratory data: CBC, BUN, PBI, T-3 resin uptake, calcium, phosphorus, amylase, lipase, SGOT, LDH, Bilirubin, and protein electrophoresis were normal as was the serum carotene and 5-hour xylose excretion. The ECG showed low T-waves and the presence of U-waves. 24-hour urinary FSH was positive at 6-mouse units and vaginal mucosal cells revealed adequate estrogen effect. The initia serum electrolytes were sodium 131, potassium 2.5 CO_2 content 28.5, and chloride 88 mEq/L. Urinalysis revealed a S.G. 1.031 p^H 8.0, no protein, and a negative sediment. Arterial blood gases showed a p^H of 7.54, $p^{co}2$ 40mm., $p^{o}2$ 97mm. The urinary potassium was only 2.5 mEq/24 hours. Because of the severe hypokalemia with metabolic alkalosis additional studies were performed. 8:00 a.m. and 5:00 p.m. cortisol levels were 21 and 20 mcg/100ml., respectively. The cortisol rose to 51 mcg/100ml. following 25 units ACTH i.v. over 5-hours. 17-ketosteroids were 5.4mgm. and 17-hydroxysteroids were 15.4/mgm/24-hours. Supine plasma renin activity was normal while the patient was hypokalemic and on a diet containing 120mEq. of sodium per day. Aldosterone excretion was 5.5mcg/24-hours, also a normal value.

In view of the unexplained electrolyte derangement the patient was re-questioned about cathartic ingestion and her bowel habit. She finally admitted to taking several Carter's Little Pills® daily for the previous 4-years and having four to five watery bowel movements daily. Table 1 contains the initial blood gas values along with sequential electrolyte determinations while the patient was consuming a regular hospital diet and taking no cathartics or potassium supplements. After being cautioned about the use of cathartics the patient gained 8-lbs. and had a marked increase in strength and sense of well-being over the ensuing 2 months.

Discussion:

Carter's Little Pills® contain aloes and podophyllum resin. Goodman and Gilman[1] describe aloe as the dried juice of leaves of various species of the aloe plant. The active principle is aloin which yields an anthraquinone derivative upon hydrolysis in the intestine. Aloe is an extremely irritating

TABLE 1

RESULTS OF BLOOD GAS AND ELECTROLYTE VALUES

Hospital Day	1	2	6	9
Sodium	131	137	138	134
Potassium	2.5	2.7	3.2	3.8
$C^{o}2$ Content	28.5	31	27	23
Chloride	88	94	98	102
p^H	7.54			
$p^{co}2$	40			
$p^{o}2$	97			

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cathartic and is accompanied by abdominal cramping and pelvic congestion. Despite contrary opinion, no action on the formation or excretion of bile has been shown.[2] Thus in more recent years the "Liver" has been deleted from Carter's Little Liver Pills®. Podophyllum resin is obtained from the roots of a plant commonly known as the Mandrake. The cathartic effect is exerted by an irritant cytotoxic effect on the intestinal tract and accompanied by the loss of sodium and potassium via the bowel. The extent of this effect is dose related. Schwartz and Relman[3] in an early study pointed out the association of hypokalemia to aloin-containing cathartic ingestion. In their patients no metabolic alkalosis was present despite the marked hypokalemia. A low urinary potassium and an elevated fecal potassium of 50-55 mEq/L was found in careful balance studies. Poor urinary concentrating capacity was ascribed to the hypokalemia. Other studies comment on the use of cascara[4] and other purgatives[5,6] as a cause of hypokalemia. Several women taking a proprietary laxative containing podophyllum resin were found to have hypokalemia.[7] The clinical picture either alone or together with the electrolyte abnormalities have suggested a myriad of diagnoses. These include Crohn's disease, ulcerative colitis, vascular colitis, Conn's syndrome, Bartter's syndrome, Addison's disease, and potassium-losing nephritis. Potassium depletion has been so severe on occasion to have the patient present with marked muscular weakness and even paralysis. Plum et al[8] described x-ray changes secondary to cathartics which were suggestive of burned out enterocolitis and showed smooth tapered areas of colonic narrowing. The "cathartic colon" with dilated bowel, loss of haustral markings and pseudo-stricture formation has been well described.[7] Cathartic induced protein-losing gastroenteropathy has recently been reported.[9]

Our patient presented with several interesting findings, including weight loss, which was probably caused from inadequate food intake along with increased daily fecal bulk. The low potassium and associated metabolic alkalosis were undoubtedly secondary to bowel loss of potassium due to cathartic abuse. The findings of low urinary potassium and the rapid rise in serum potassium on a normal hospital diet, once cathartics were stopped, support this view. Increased aldosterone secretion is unlikely because of the normal aldosterone excretion together with the plasma renin value. The patient underwent previous surgery because of lower abdominal pain which could have been caused by cathartic induced intestinal cramping of pelvic congestion or the combination of these factors. The melanin pigment found in the appendix may be the result of previous cascara ingestion,[10] although the patient denies this possibility. The amenorrhea remains a vexing problem. The often seen association of amenorrhea with weight loss and poor nutrition is the most likely possibility. Although FSH was present on one determination, the well known variability of daily urinary bioassay FSH values[11] make it possible that FSH was undetectable most of the time. It is tempting to speculate that prolonged pelvic congestion due to the aloin might in some way inhibit ovulation.

In any unexplained case of hypokalemia with or without alkalosis cathartic abuse must be suspected. This is especially true in women who may emphatically deny taking medication or having an abnormal bowel habit.

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Generic and Trade Name of Drug

Aloes and podophyllum resin—Carter's Little Pills

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Serum Antinuclear Antibodies in Rheumatoid Arthritis

Grace D. Hughes, M.D. and Naomi F. Rothfield, M.D.

With the application of the immunofluorescent method of demonstrating antinuclear antibodies (ANA), there have been many and varied reports on the incidence of these antibodies in patients with rheumatoid arthritis. Investigators have reported that there is a 2 to 5% incidence of ANA in the normal population (1-4). In patients with systemic lupus erythematosus (SLE), however, the incidence is reported as being from 97 to 100% (1, 2, 5, 6). ANA have been found in other collagen diseases as well as in myasthenia gravis, thyroid diseases, ulcerative colitis, and liver diseases (1, 7, 8). The incidence of ANA in rheumatoid arthritis has been cited as from less than 10% to as high as 65% by various authors (1, 2, 4, 6-15).

The purpose of this report is to describe the incidence, titer, class, and pattern of ANA in a group of patients with rheumatoid arthritis and to compare these results to those obtained previously in this laboratory in patients with SLE and progressive systematic sclerosis (PSS).

Materials and Methods

Serum was obtained from 100 patients with rheumatoid arthritis who were either hospitalized in Bellevue Hospital or attending the New York University Arthritis Clinics of Bellevue Hospital. All patients fulfilled the criteria (A.R.A., revised 1958) for definite or classical rheumatoid arthritis. The Steinbrocker classification was used to determine the severity of the disease process (16). Seventy-two females and 28 males were studied, ranging in age from 18 to 72 years. The disease durations varied from three months to more than 20 years Fifty-five patients were in Stage 1 or 2 and 45 in Stage 3 or 4 (Steinbrocker's Classification).

ANA were detected by the indirect fluorescent technique using rabbit anti-human γ-globulin conjugated to fluorescein isothiocyanate and cryostat-cut sections of mouse liver as a source of nuclei, as previously described (17). Titers were performed on all available sera which were positive when tested undiluted. Twenty of the positive sera were not available in sufficient quantity, and titers, therefore, could not be performed on these sera. Positive sera were also tested for the presence of IgG and IgM ANA using mono-specific rabbit anti-human Fc fragment conjugated to fluorescein isothycianate and rabbit anti-human IgM conjugated to fluorescein isothycanate. Slides were graded as negative or 1-4 plus, according to the intensity of fluorescence. Sera giving a positive test were then titered to determine the maximum titer at which fluorescence could be observed.

The latex fixation test was performed by the method of Singer and Plotz (18). LE preparations were performed by the method of Zimmer and Hargraves (19).

Results

Incidence and Titer

Sixty-six percent of the sera gave a positive test for ANA when tested undiluted. A weakly positive (1+) reaction was produced by 19 sera (19%), and a moderately or strongly positive (2-4+) reaction was produced by sera from 47 patients.

Titers were performed on 46 of the 66 positive sera (Table 1). Thirty-three of the 46 positive sera had titers of 1:8 or less. Thirteen sera gave titers from 1:16 to 1:512. Thus, 40% of the positive sera on which titers were performed had titers of from 1:16 or greater. Thirteen of the 46 sera had reactions of 1+ when tested undiluted. Of these, five were positive only when tested undiluted; four were positive at 1:1, two at 1:2, and two at 1:4 dilutions (Table 1). Thus, since no sera giving a 1+ reaction when tested undiluted had a titer of 1:16 or greater, the remaining data are based on the reactions in sera giving a reaction of greater than 1+. Of the

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100 sera tested, 47 had a moderately or stronger positive test (greater than 1+) when tested undiluted.

No correlation could be demonstrated for the presence of ANA and longer disease duration. Fifty percent of the 22 patients whose disease duration was less than 4 years had a greater than 1+ ANA test and 50 percent of 24 patients whose disease duration was greater than 20 years had a greater than 1+ ANA test.

TABLE 1

TITERS OF ANA IN SERA FROM 46 PATIENTS WITH RHEUMATOID ARTHRITIS

Titer	*No.*
Undiluted	6
1:1	9
1:2	5
1:4	13
1:8	0
1:16	2
1:32	4
1:128	3
1:256	2
1:512	2
TOTAL	46

TABLE 2

RELATION OF ANA TO AGE OF PATIENT WITH RHEUMATOID ARTHRITIS

Years	*No. Patients*	*+ ANA > 1+* *No.*	*%*
0-20	2	0	0
21-40	16	8	50
41-60	55	26	47
>60	27	13	48

No correlation could be demonstrated between age of patients and incidence of ANA (Table 2). A slightly higher incidence of ANA was found among the female patients (53%), than among the male patients (31%), but was not statistically significant.

Sera from patients with more severe disease were found to have a slightly higher incidence of ANA than sera from patients with mild disease although the numbers in each group are small. In addition, higher titers of ANA were present in sera from patients with more severe disease (Fig. 1). When titers of ANA in the rheumatoid arthritis patients were compared with titers previously reported from this laboratory in patients with SLE and PSS (20), the titers in the rheumatoid arthritis patients were lower (Fig. 2).

Pattern

The diffuse pattern of nuclear fluorescence was observed twice as often as the speckled pattern, using the undiluted sera. At higher titers, some sera lost the diffuse pattern and a speckled pattern was revealed. The type of pattern observed could not be correlated with stage of disease or presence of rheumatoid factor (Table 3).

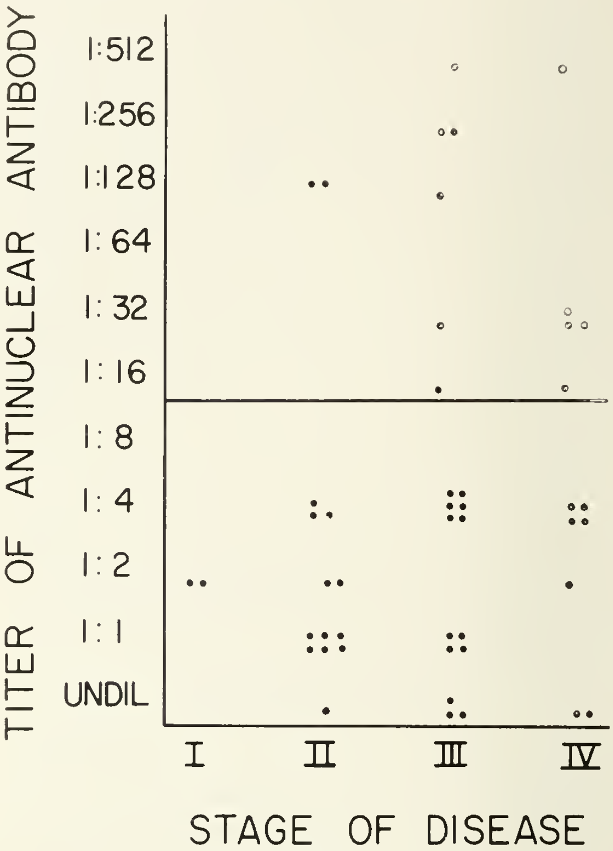

Figure 1

Relation of Titer of Antinuclear Antibody to Stage of Disease.

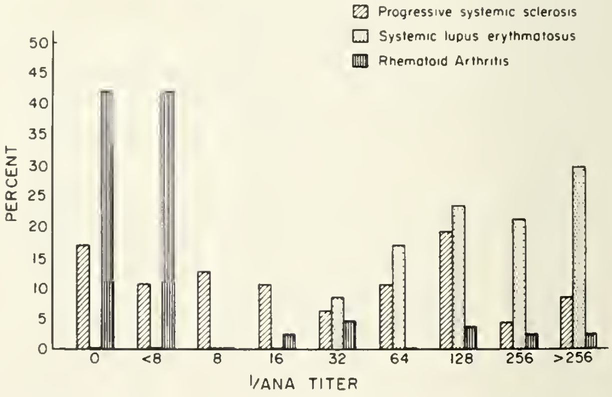

Figure 2

Serum Antinuclear Antibody Titers in Progressive Systemic Sclerosis, Systemic Lupus Erythematosus and Rheumatoid Arthritis.

The peripheral pattern was produced by sera from two patients. One patient had rheumatoid factor and a positive LE cell preparation and had rheumatoid arthritis for 21 years. She was classified as Stage 4 and had no symptoms suggestive of SLE.

TABLE 3

RELATION OF PATTERN OF ANA TO RHEUMATOID FACTOR AND STAGE OF DISEASE (RHEUMATOID ARTHRITIS)

Type of Pattern	*Total No. Patients*	*+RF*	*Stage of Disease*	
			1-2	*3-4*
DIFFUSE	47	30	23	24
SPECKLED	17	7	10	7
PERIPHERAL	2*,**	1**	1*	1**

* Patient had a history of pleuritis and negative LE preparations at the time of study. Six months later she developed pleural effusion, erythematous butterfly rash, and Raynaud's phenomenon.

** Patient had no symptoms of SLE but had a positive LE preparation. No symptoms have subsequently appeared suggestive of SLE.

The other patient in whom a peripheral pattern was found had a negative test for rheumatoid factor, negative LE preps, and a history of pleuritis at the time the blood was obtained. She developed an erythematosus rash and Raynaud's syndrome during the following six months.

The pattern of nuclear fluorescence produced by undiluted sera from patients with rheumatoid arthritis is compared with the predominant patterns produced from patients with other rheumatic diseases, normal individuals, and patients with chronic discoid lupus erythematosus (Table 4). The diffuse pattern is found most frequently in sera from patients with rheumatoid arthritis, discoid lupus erythematosus, and SLE. In the other diseases, a speckled pattern is most commonly observed.

TABLE 4

INCIDENCE OF ANA

Group	*Total No.*	*No. +ANA*	*% Positive*	*Predominent Pattern*	*% >1+*
Normals	216	15	6	Speckled	2.3
R.A.	100	66	66	Diffuse	47
PSS	47	39	82	Speckled	68
SLE	200	200	100	Diffuse or Peripheral	98
Discoid L.E.	44	11	25	Diffuse	11
Dermatomyositis	15	8	53	Speckled	62
Polyarteritis	12	5	42	Speckled	40

Immunoglobulin Class of ANA

The class of immunoglobulin ANA was determined in sera from 44 patients. Thirty-six had IgM ANA and 18 had IgG ANA. Sera from 26 patients had IgM ANA but no IgG, and seven had IgG but no IgM ANA. Sera from 11 patients had both immunoglobulin classes of ANA.

The class of ANA in 44 patients with rheumatoid arthritis is compared to the class found previously in 47 patients with PSS (20) and 100 patients with SLE (21) in Table 5. IgM ANA was present in 84% of rheumatoid arthritis patients as compared to 81% with SLE and only 18% with PSS. IgM was the only immunoglobulin class of ANA in 59% of the rheumatoid arthritis patients as compared to only 14% of the PSS and 4% of the SLE patients.

The relation of the immunoglobulin class of ANA to the presence of rheumatoid factor and disease duration in patients with rheumatoid arthritis is shown in Table VI. Of the 26 patients who had only IgM ANA, 22 had their disease for 4 years or longer. A positive latex fixation test was present in only 12 of 26 patients with only IgM ANA, 2 of

TABLE 5

INCIDENCE OF IMMUNOGLOBULIN CLASS OF ANF IN R.A., SLE, AND PSS

	R.A.	*PSS*	*SLE*
Total No. Pts.	44	47	100
% IgM	84	18	81
% IgG	40	86	96
% Only IgM	59	14	4
% Only IgG	16	18	18

TABLE 6

RELATION OF IMMUNOGLOBULIN CLASS OF ANA TO RHEUMATOID FACTOR AND DISEASE DURATION

Immunoglobulin Class of ANA	*No. Patients*	*+RF*	*Disease Duration*	
			0-3 Yrs.	*4 Yrs. & Over*
Only IgM	26	12	4	22
Only IgG	7	2	3	4
IgG + IgM	11	10	2	9

TABLE 7

RELATION OF IMMUNOGLOBULIN CLASS TO STAGE OF DISEASE

Immunoglobulin	*Total No.*	*Stage*	
		1-2	*3-4*
Only IgM	26	14	12
Only IgG	7	4	3
IgG + IgM	11	2	9

7 patients with only IgG ANA, and was present in ten of 11 patients who had both IgG and IgM ANA.

There was no correlation between class of ANA and stage of disease (Table VII) although nine of 11 patients with both immunoglobulin classes of ANA were in Stage 3 or 4 and were the same patients who had a positive latex fixation test and disease duration of four years or longer.

LE Cell Preparations

Only two patients had a positive LE cell preparation. In both, IgG ANA was present, and the pattern was diffuse in one and peripheral in the other (see above).

Discussion

The immunofluorescent ANA test is more frequently positive in rheumatoid arthritis than is the LE cell test. The variation in reported incidence of ANA between different centers of investigation is wide and may, in part, be attributed to the many different techniques in use (Table 8). The substrate may consist of leukocyte smears (1, 2, 6, 9, 10) cryostat sections of human thyroid (11-13), mouse liver (14), human skin (15), or imprints of tumors (8). These differences as well as the differences between the groups of cases studied probably play a part in contributing to the variation.

In 1959, Duthie found a 47% incidence of ANA in 264 cases of rheumatoid arthritis studied. He also noted an increased incidence in females over males and that there were fewer positives in patients with disease of short duration (10). In 1960 Hall et. al. (15) cited an incidence of 36% ANA out of 130 patients tested. In patients with scleroderma, polyarteritis nodosa, and dermatomyositis, the positive ANA were correlated with the activity of the disease. These investigators also suggested that the

TABLE 8

INCIDENCE OF ANA IN RHEUMATOID ARTHRITIS — SUMMARY OF PREVIOUS INVESTIGATIONS

Study	*No. Tested*	*% Positive*	*Substrate*	*TITERS*				*Misc.*
				1:10	1:10-1:100	1:100-1:500	1:1000	
Duthie et al., 1959 (10)	264	47	Human Leukocytes					
Alexander et al., 1960 (6)	183	65	Human Leukocytes					Titer 1:64 in 11%
Hall et al., 1960 (15)	130	36	Human skin					
Weir et al., 1961 (12)	132	10	Human Thyroid	8%	75%	16%		
Seligmann, 1965 (14)	107	61	Mouse liver	17%	16%	27%	1%	
Hasker et al., 1965 (1)	58	70	Leukocytes					10% bright homogen. 60% dull speckled
Barnett et al., 1965 (2)	59	30	Leukocytes					Mean titer 32
Condemi et al., 1965 (9)	68	35	Leukocytes	52%	47%			
Faber, Elling, 1965 (11)	100	30	Thyroid	36%	63%			
Burnham et al. 1966 (8)	42	73	Tumor Imprint					9/30 strongly positive
Onoder et al., 1966 (7)	250	8	Nucleoprotein Compl. Fix.	70%	15%	5%	10%	
Corbett et al., 1967 (13)	120	47	Thyroid					

ANA negative rheumatoid sera might give a positive reaction if their euglobulin fraction was used for the test (15). Seligmann (14) using mouse liver as substrate, found 61% positive ANA which is very similar to our finding of 66% positive using the same substrate.

Barnett et. al. and Condemi et al. in two different studies, reported a 35% incidence of positive ANA in rheumatoid arthritis (2, 9). In these studies they also noted that patients with the most severe disease had the higher incidence of ANA. In comparing the data obtained in this laboratory on patients with SLE and PSS, it was noted that in rheumatoid patients, the titers were much lower. Nevertheless, those with higher titers were found among those with the most severe disease (Fig. 1). Barnett et al. found that IgM ANA generally appeared early in the disease and noted that this was similar to the normal sequence of antibody from immunization with foreign or autologous antigens. In their study the patients who had positive LE preps were found to have IgG ANA most frequently. Our series included only two patients with positive LE preps. Both of these had IgG ANA present. Unlike Duthie or Barnett, we could not correlate a positive ANA with prolonged disease duration.

There was a 6% incidence of positive ANA in undiluted sera from 216 normals studied in our laboratory. It should be noted that a very small number of normals were greater than 1+. In this group, the predominant pattern seen was overwhelmingly that of a speckled type (Table 4). This contrasts greatly with the more frequent diffuse pattern seen in rheumatoid arthritis and SLE (3, 21).

Summary

Sera from 100 patients with rheumatoid arthritis were studied for the presence of ANA by the fluorescent antibody technique, and the results correlated with the clinical data on the patients. Sixty-six percent of the patients' sera had a positive ANA test using undiluted sera with 47% giving a greater than 1+ reaction. There was no correlation between presence of ANA and disease duration. There was no difference in incidence of ANA between the rheumatoid factor positive patients and those without rheumatoid factor. The ANA was slightly higher in females than in males, but this was not significant. There was an increased incidence of ANA with advanced stage of disease. The diffuse pattern was seen twice as often as the speckled pattern. The pattern of nuclear fluorescence could not be correlated with age, sex, presence of rheumatoid factor, or stage of disease. IgM immunoglobulin was most frequently present. Titers of ANA in rheumatoid arthritis were found to be lower than titers found in SLE and progressive systemic sclerosis.

Acknowledgments

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Reports On Fluoridation Study

Controversy over the efficacy of fluoridated public water supplies has not abated, according to findings of a special fluoridation study committee of the Fairfield County Medical Association.

The reports were accepted at the association's semi-annual meeting in October. According to a member of the committee, Robert Fand, M.D., Danbury, comments in both the majority report and his own minority report support his position about possible adverse effects of fluoridation.

For an objective evaluation of the arguments on each side, both reports are printed in full.

Majority Report

1. Interesting and provocative research on this broad and complex subject, worthy of attention, is proceeding in many parts of the world. A report from Stuttgart, Germany, for example, indicates that some foods may be enriched by uncontrolled fluorides in the air and water. This fluoride multiplication factor, since it raises the further issue of the known and unknown pollutant elements in our environment, may not properly be within the narrow purview of this Committee.

2. The dental profession and its spokesmen, the American Dental Association, feels strongly that controlled fluorides are helpful in the prevention of dental caries in children up to the age of 10 years.

3. Bone structure in all age levels of our population appear to derive benefit from fluoridated water.

4. On the basis of present scientific evidence and knowledge the Committee concludes that there is no reason for concern about adverse effects from the use of fluoridated community water supplies.

Minority Report

1. We feel continuation of *controlled* fluoridation of our drinking water should be endorsed at this time. The FDA has indicated a limit of 2 mg of total fluoride intake per day.

2. The dental profession feels strongly that fluorides are very helpful in the prevention of caries in children until the age of 10 years.

3. On the basis of present scientific evidence and knowledge we find no reason for concern about adverse effects from use of fluoridated community water, provided the total intake per day from water and solids does not exceed 2 mg per day.

4. A controlled study of fluoride consumption should encompass all possible sources of intake. Its study of the pertinent literature has convinced the Committee that a toxic fluoris is both a definite reality and a potential hazard. The dangers are those of fluoride multiplication through the reconstitution of dried or concentrated food products with fluoridated water and biological enrichment through air pollution and irrigation with fluoridated water.

5. It behooves the State Department of Health to set up the proper testing facilities to protect the Connecticut consumer from the possibility of fluorosis.

Reliability of Diagnostic Tests in Patients With Carcinoma of the Lung

Charles E. Morhardt, M.D. and Ernest J. Montgomery, M.D.

There are several tests which can be used to assist the clinician in the diagnosis of carcinoma of the lung. Among these are scalene node biopsy and cytologic study of sputum, bronchial washings and pleural fluid. How well do these tests correlate with each other and with subsequent more definitive biopsy at thoracotomy or bronchoscopy?

In an effort to provide answers to this question, the records of all patients assigned a diagnosis of carcinoma of the lung at the Western Pennsylvania Hospital during a six year period, 1958-1963, were studied. There were 375 cases assigned this diagnosis, but only 246 patients had histologic confirmation of the diagnosis at thoracotomy, bronchoscopy or autopsy. Subsequent studies were restricted to the latter group.

Material and Methods

The tumors were classified into four groups on the basis of the histologic appearance of the biopsy specimen (Table 1). Each of the four tumor types were further analyzed with respect to age and sex incidence (Table 2), and the diagnostic reliability of scalene node biopsy, and cytologic examination of sputum, bronchial washings and pleural fluid.

TABLE 1

HISTOLOGIC DIAGNOSIS IN 246 PATIENTS WITH CARCINOMA OF THE LUNG AT THE WESTERN PENNSYLVANIA HOSPITAL

Type of Tumor	*# of Cases*	*% of Total*
Epidermoid	108	44%
Small Cell	73	30%
Large Cell	27	11%
Adenocarcinoma	38	15%
TOTALS	246	100%

Sputum and bronchial washing specimens were stained by the Papanicoleau method after collection in 50% ethyl alcohol. The results were reported in four classes as follow: Class I—negative for malignancy; Class II—atypical cells present; Class III—suspicious for malignancy; and Class IV—malignant cells present. Pleural fluid was collected in a sterile container, centrifuged, and cell blocks were made.

Results

Scalene node biopsies were performed in 132 patients with an overall yield of positive histologic diagnosis of tumor in 36% of the biopsies. Table 3 defines the results in relation to the histologic variant of tumor studied. Generally, scalene node biopsies were performed prior to thoracotomy in an attempt to secure an accurate diagnosis and possibly avoid a thoracotomy.

Cytologic examination of the sputum was performed in 206 of the cases studied, with a 42.8% overall incidence of positive (Class IV) sputums. This is further explained according to specific histologic tumor types in Table 4.

Cytologic examination of the bronchial washings was performed in 170 patients with an overall incidence of 35.3% positive (Class IV) results. The relationship of this finding to the specific histologic type of tumor is elaborated upon in Table 5.

Results of examination of the pleural fluid was next studied. Twenty-one patients in this series were subjected to examination of their pleural fluid by cytologic techniques. Nine patients had a diagnosis of malignancy made on this basis. Table 6 defines the results in relation to tumor type.

Discussion

Many of the patients in this study had advanced disease when the diagnostic tests were performed. The tumors were considered non-resectable if metastases were demonstrated, if malignant cells were present in the pleural fluid or if vocal cord paralysis was present. Other reasons for not resecting a tumor were if the patient refused surgery (two instances in this study) or if the patient was considered an extremely poor operative risk. The resectability rate for each cell type was as follows: epidermoid carcinoma, 22%, undifferentiated; small cell carcinoma, 7%, undifferentiated; large cell carcinoma, 15%; and adenocarcinoma, 16%.

DR. CHARLES E. MORHARDT, Courtesy with assignment—Hartford Hospital, Hartford, Conn.

DR. ERNEST J. MONTGOMERY, U.S. Army, Former resident in surgery, Western Pennsylvania Hospital, Pittsburgh, Pennsylvania.

From the Department of Surgery, Hartford Hospital, Hartford, Conn.

TABLE 2

AGE AND SEX INCIDENCE OF 246 PATIENTS WITH CARCINOMA OF THE LUNG

Tumor Type	*Sex*	*20-29*	*30-39*	*40-49*	*50-59*	*60-69*	*70-*	*Total*
Epidermoid	Male	1	1	8	35	38	14	97
Carcinoma	Female	0	1	3	3	3	1	11
Small Cell	Male	0	2	7	16	24	10	59
Carcinoma	Female	0	1	4	1	8	0	14
Large Cell	Male	0	2	4	6	12	2	26
Carcinoma	Female	0	0	0	0	1	0	1
Adeno-	Male	0	0	7	7	15	2	31
carcinoma	Female	0	1	0	2	1	3	7
TOTALS	Male	1	5	26	64	89	28	213
	Female	0	3	7	6	13	4	33

Although scalene node biopsy was not positive in 72% of the patients with epidermoid carcinoma, the resectability rate was only 22%. Similarly, the incidence of negative scalene node biopsies in small cell carcinoma was 52%, but only 7% of the tumors studied were resectable.

These results are similar to the reports by Blair and Hughs (1). In 1961, they reported a 26.5% incidence of positive scalene node biopsies, while in 1966 their overall yield dropped to 16% positive biopsies. The average time from the date of diagnosis to death was approximately three months after scalene node biopsy. They conclude that this procedure is of questionable help in altering prognosis.

TABLE 3

RESULTS OF SCALENE NODE BIOPSIES PERFORMED IN 132 PATIENTS WITH CARCINOMA OF THE LUNG

Tumor Type	*Scalene Node Biopsies Performed*	*Number of Positive Biopsies*	*% Positive*
Epidermoid	50	14	28
Small Cell	44	21	48
Large Cell	16	1	6
Adenocarcinoma	22	12	46
TOTALS	132	48	

Shields and Shocket reported a 7% incidence of positive scalene node biopsies in their study on preoperative evaluation of patients with clinically resectable bronchogenic carcinoma (2).

It was also the impression of Blair and Hughs that undifferentiated tumors metastasize to scalene nodes more readily than epidermoid carcinoma. This agrees with the present study except in the case of large cell undifferentiated tumors. They felt that adenocarcinoma spread to the scalene nodes infrequently, but we found a 46% incidence. Horwitz and Findlay also report a high incidence of positive biopsies in adenocarcinoma (3).

Class IV results were reported in 43% of the sputum specimens and 35% of the bronchial washing specimens. Adenocarcinoma yielded the lowest number of positive results with both tests, while epidermoid carcinoma yielded the highest percentage of positive results. No data is available on false positive sputum cytologic reports during this period, but it would appear that examination of the sputum is just as good, if not better, than examination of the bronchial washings in suggesting a diagnosis of carcinoma of the lung.

This study correlates fairly well with the study of Ozgelen, et al (4). In 415 cases af carcinoma of the lung cytologic examination was positive in 41% of sputum specimens, 32% of bronchial secretions, and 51.3% of pleural fluid specimens.

Liebow, Lindskog, and Bloomer report positive cytologies in 42.8% of sputums and 30% of the bronchial washings studied (5). This again correlates well with the present study.

However, other workers have reported a higher incidence of postive sputums. Papanicoleau, in 1946, reported an incidence of 69% (6). Herbut and Clerf reported a figure as high as 82% positive cytology in their study of 57 cases of cytologic examination of bronchial secretions (7). McKay, Ware, Atwood and Harken, studying the diagnosis of lung cancer by smears obtained from bronchoscopic aspirations reported 40 instances of positive cytology in 54 cases of carcinoma of the lung for an overall incidence of 74% (8). They found that the smear was positive in 26% of the cases that were negative at bronchoscopy.

Since pleural fluid is usually considered a sign

TABLE 4

RESULTS OF CYTOLOGIC EXAMINATION OF THE SPUTUM
IN 206 CASES OF CARCINOMA OF THE LUNG

Tumor Type	*Class I*	*Class II*	*Class III*	*Class IV*	*Total*
Epidermoid	12 (13%)	28 (30%)	8 (8%)	46 (49%)	94
Small Cell	14 (23.3%)	15 (25%)	9 (15%)	22 (36.7%)	60
Large Cell	3 (14%)	7 (32%)	2 (9%)	10 (45%)	22
Adenocarcinoma	10 (34%)	7 (24%)	2 (6%)	11 (36%)	30

TABLE 5

RESULTS OF BRONCHIAL WASHINGS CYTOLOGY
IN 170 CASES OF CARCINOMA OF THE LUNG

Tumor Type	*Class I*	*Class II*	*Class III*	*Class IV*	*Total*
Epidermoid	25 (30%)	17 (20%)	8 (9%)	35 (41%)	85
Small Cell	17 (40%)	10 (23%)	6 (14%)	10 (23%)	43
Large Cell	8 (42%)	3 (16%)	0	8 (42%)	19
Adenocarcinoma	12 (52%)	3 (13%)	1 (4%)	7 (31%)	23

of advanced disease, it was surprising that only 9 of 21 patients had cytologic confirmation of neoplastic cells in the pleural aspirate. Indeed, only one of eight patients with oat cell carcinoma and pleural effusion yielded a positive cytologic diagnosis.

These studies tend to confirm the impression that each of the tests examined have a definite place in the diagnosis and treatment of the patient with a suspicious lung lesion. True positive results can be expected in less than half of the patients, but unnecessary operation can be avoided in many of the patients who otherwise would have been subjected to thoracotomy. Conversely, a positive sputum or bronchial washing cytology led the surgeon towards the diagnosis of malignancy in many cases and thereby prompted earlier operation and presumably a greater chance of cure.

Summary

In 246 patients with a positive histologic diagnosis of carcinoma of the lung, a retrospective study has determined the correlation of various diagnostic tests. Scalene node biopsy was positive in 36% of the cases. Sputum cytology was positive in 43% of the cases, and bronchial washing cytology was positive in 35% of the cases. Pleural fluid cytology was positive in 43% of the cases studied.

All tests were most often positive in the epidermoid variety of lung cancer. Adenocarcinoma yielded the lowest percentage of positive results, and the undifferentiated small cell and large cell cancers were in an intermediate group.

TABLE 6

RESULTS OF EXAMINATION OF THE PLEURAL FLUID
IN 21 CASES OF CARCINOMA OF THE LUNG

Tumor Type	*Pleural Fluid Aspirations*	*Number With Positive Cytology*
Epidermoid	6	3
Small Cell	8	1
Large Cell	2	1
Adenocarcinoma	5	4
Totals	21	9

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Puncture Wounds in Surgical Gloves

William C. Butterfield, M.D.

Introduction

It has long been known that leakage of bacteria through a glove puncture can be a source of wound infection. In the 1890's, surgeons recommended the use of long instruments so that the gloved hand, liable to damage by manipulations during an operation, would not come into contact with the wound. In more recent times, Devenesh and Niles[2] in an investigation of hospital infections where the source turned out to be a surgeon carrying staphlococcus aureus, pin pointed the mechanism of spread to glove punctures. Colony counts obtained from this surgeon's gloves post-operatively ranged from five to 5,000. From another surgeon who was not a source of infection and therefore served as control, bacterial counts were consistently under one hundred and were never staphlococcus aureus. The extent of the bacterial count also correlated with the wetness of the gloves. In another study Wise and co-workers[6] isolated staphlococci from the interior of 90% of 481 surgical gloves cultured at the conclusion of the surgical procedure. Coagulase positive staphlococci were isolated from 14%. Cole and Bernard[1] in an experimental study made punctures with a #18 needle, and when the punctured finger was placed in sterile blood for 20 minutes, 28% of the group produced staphlococcus aureus counts ranging from 4,000 to 18,000. It is apparent, therefore, that glove punctures in contact with blood or sweat, are a source of bacterial contamination. Though the data is not extensive it is recognized that a surgeon may serve as a source of wound infection as a result of glove damage if he is a carrier of staphlococcus aureus. With this background in mind, the following study was carried out. Its main purpose was to determine the frequency of glove punctures during surgery. It was hoped that additional data correlating punctures and infections might be obtained.

Methods

One hundred consecutive operations were analyzed. All specialty procedures were included though most were general surgical problems. At the end of each operation, the gloves of all participants were collected. Identification of all gloves as to surgeon, assistants, nurse and the name of the operation was made with an idelible marker. The gloves were then inflated with a small air pump and placed under water. Any leak large enough to bubble was counted and multiple punctures in one glove were tabulated separately. The locations of punctures were also noted. The type of operation, its duration, the number and location of the puncture wounds and the people whose gloves were involved were recorded on a master sheet.

Results

There were a total of 190 separate punctures in the 100 operative cases analyzed. (1.9 punctures/case) The surgeon accounted for 56%, the first assistant 16 and the scrub nurse 26 of the punctures. Almost half the surgeon's punctures were in the index finger with the left being the most frequently damaged. The next most common location was the thumb where, once again, the left side predominated.

70% of the operations had one or more glove perforations. The number ranged from one to 11 and correlated grossly with time. Twenty-nine of thirty operations with *no* punctures were two hours or less in duration with two-thirds of these one or less hours. On the other hand, thirty of the seventy operations with punctures were two or more hours. With one exception, all studies of two or more hours had at least one puncture. The three longest procedures, a portocaval shunt, a plastic reconstruction of the nose utilizing a forehead flap and a radical neck dissection with mandibulectomy, had seven, eleven and eight punctures respectively.

Discussion

These findings are similar to operations made by others. Shouldice and Martin[4] in a study of 330 hernia repairs found 61% of the operations had punctured gloves. Russell, et al,[3] testing gloves with an electrical device, found at least one defective glove in 79% of operations. This figure increased to 85% for cases lasting longer than one hour and decreased to 55% in cases under one hour. It was also noted that the most common cause of wound infection, staph epidermides, was the most common organism cultured from fingers after the surgical scrub and post-operatively. No attempt, however,

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DR. WILLIAM C. BUTTERFIELD, Assistant Professor of Surgery, University of Connecticut Health Center, McCook Hospital, 2 Holcomb Street, Hartford; Consultant in Thoracic Surgery, Veterans Administration Hospital, 555 Willard Avenue, Newington.

was made to correlate punctures with infected cases. In our study there were three post-operative infections and ironically, two of the three were in operations free of punctures. Russell, et al, also noted that the surgeon's gloves accounted for the most punctures on the surgical team, and the left index finger was the most frequently involved followed by the left thumb. We believe this to be the result of holding the needle between thumb and index finger when placing it in the needle holder. The use of forceps during this maneuver, might eliminate such tears. As to glove punctures located elsewhere, it is suggested that, since the number increases with the duration of the operation, a change of gloves on an hourly basis for the surgeon, scrub nurse and probably the first assistant should be instituted. Although direct proof of a cause and effect relation between punctures and infection is lacking, it is known that both vary directly with the length of the procedure.[5]

Finally it is hoped that this report will stimulate glove manufacturers to further research. It is obvious that the ideal lightweight elastic material has yet to be found.

Summary and Conclusions

Seventy of 100 surgical procedures were found to have at least one glove perforation. The number of perforations per case increased as operating time increased. The surgeon's gloves were the most frequently involved.

Corrective measures, including instrument technique, frequent glove changes and research into more durable materials has been suggested.

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THE PRESIDENT'S PAGE

MALPRACTICE

No one can deny the fact that the practice of medicine is constantly faced with decisions, frustrations and challenges of all kinds. Were medicine an exact science like mathematics, our problems could be resolved promptly with due precision, and be far less in number and magnitude. But *medicine* is *not* an exact science, notwithstanding some writers and some of the uninformed or misinformed public. Instead, our profession is a biological science (also an art) with phenomena in a "constant state of flux." With skill, adequate instrumentation, experience and a mature sense of judgment, our medical diagnostic and therapeutic problems become greatly simplified. But one soon learns that the image of the physician before the public does not depend entirely upon that pragmatic approach. During the past two decades, our lot and prestige has worsened by an ever increasing number of malpractice suits.

What is a malpractice suit or better yet, what is malpractice? Jetter[1,2] (from Black's Law Dictionary) defines malpractice as "bad, wrong, or injurious treatment of a patient professionally, resulting in injury, unnecessary suffering or death to the patient and proceeding from ignorance, carelessness, want of proper professional skill, disregard of established rules or principles, neglect or a malicious or criminal intent." Malpractice may be either criminal or civil. According to Gonzales[3] and others, four points must be proven in order for a malpractice action against a physician to be valid court action. They are often referred to as the four "D's." In natural order, they are (a) Duty (to injured person), (b) Dereliction (of duty), (c) Direct Causation and (d) Damage (physical) to patient. All four points must be proven by the plaintiff.

The natural question of our readers is why "all this fuss and concern? We've had malpractice suits for years; the patient must be protected and the guilty physician be punished." Quite true. As a matter of fact, the first malpractice suit in the United States was recorded against a Connecticut physician in 1794.[4] And there have been many before and since the Civil War.[5] What is alarming is the avalanche of such suits in the last two decades. According to one large writer of malpractice insurance, a leader in its own right in Hartford, it is reported that between 1963-1968, there was a national increase of 43% of medical malpractice suits—but what is significantly alarming—is that the increase in cost per case was about 200%.[6] Such costs only result in doubling or trebling insurance premiums —which in turn are passed on to the next patient in increased charges of medical services! Further, it is now clear that about one in every seven physicians in this country becomes involved in a malpractice suit in a lifetime. Aside from the intense aggravation precipitated, the harassment, public and otherwise, the loss of public image and perhaps professional stature and pride, there is loss of invaluable professional time to be devoted to other patients. It is, therefore, no wonder that some physicians have left the practice of medicine, others refuse to care for "problem cases" and still others routinely order the entire gamut of laboratory and other tests for fear of missing the one and only test that the plaintiff's lawyers might "hang him on" or rest the case on. What is also disturbing is the impression that the crescendo of malpractice cases is creating for the "would-be" physician. As one recently stated, "Why spend my entire life defending myself in court when my peers and patients check me daily?"

It must not be construed that some physicians are not guilty of malpractice—whether by accident or intent. This is true in practically every profession. The fact must be emphasized that for years, since 1790, mechanisms have been made available to protect the patient. Aside from the Hippocratic Oath, the physicians' knowledge of the code of medical ethics, there is in virtually every county medical organization in this country, a medical ethics or deportment committee, a review committee and other mechanisms for appeal. Many county and state medical organizations have legal counsel available and many have a Medical-Legal Liaison Committee. Sadusk[7] emphasized four factors which precipitate or contribute to the initiation of a malpractice suit. Briefly, they are (1) professional factors, (2) patient-physician relationships, (3) the cultural setting of our times and (4) miscellaneous, which are often difficult to evaluate. Sadusk states that "medical advances reported by the lay press have caused the public to believe that doctors are infallible; hence, if all does not go well the patient is likely to consider that his doctor was negligent. In addition, we've had a critical press during the past decade or two because organized medicine has made decisions which are not popular with press, public, or the government."

Of great concern of course, is the availability of a "contingency fee" for lawyers, special courses on how to sue physicians, a recent book on the erratic physician, and above all, the 1968 court ruling of the Supreme Judicial Court of Massachusetts which completely rejected the "locality rule.[8,9,10] Disregard of the locality rule, concerning the significance of local practice of physicians as the chief guiding principle in their practice, constituted "a blow to the defense of medical malpractice claims."

And now for therapy: Protection from malpractice suits in over 90% of the cases begins at home *and with you.* Know yourself, thy professional limitations and thy professional colleagues and interrelationships. Study the hospital rules and regulations and methods and limitations of medical practice in your city, and be cognizant of what aid the county and state medical societies and the AMA can provide. Take no chances! When in doubt, call for advice and consultation from your colleagues. Protect your patient at all times.

Finally, this Page would be incomplete if comment was not made concerning soaring malpractice premiums.[11,12] Such added costs should not be passed on to patients. Unfortunately they have to be. Increased malpractice premiums have become a national problem. Aside from the concern and effort the AMA is showing, many state medical societies have made significant strides with a measure of success, notably, Oregon, Washington and Oklahoma. Last year, Oklahoma declared a *dividend* to the physician subscribers of its own state-operated Malpractice Coverage Plan! With a little effort, determination and better professional "policing" of members, malpractice suits can be decreased and premiums can be lowered, with both the patient and the physician safer and happier. Why not in Connecticut? Your President recently took the opportunity to approach our cooperative, sympathetic and vitally interested Commissioner of Insurance, Mr. William R. Cotter, to discuss such a plan. No commitments were made except a promise to study the problem. In the meantime, we are patiently awaiting the report of the Society's Insurance Committee, under the able leadership of M. David Deren, M.D., to provide background information and recommendations for Commissioner Cotter and our Council to consider. There is much room for progress in this direction both for our patients and for physicians.

Stevens J. Martin, M.D.

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Diagnosis and Management of Hypoglycemia

Philip Felig, M.D.,
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This patient is a 42-year-old lady, admitted to Yale-New Haven Hospital on August 24th for evaluation of hypoglycemia.

She had been in excellent health all her life, until one year before admission when she noticed episodes of inappropriate behavior, dizziness, and sweating. Episodes usually occurred between 1:00 and 3:00 in the afternoon (one-half to two hours after lunch), but also occurred in late morning, particularly if she missed breakfast. She did not experience sensations of hunger, but found that eating sweets or drinking Coca Cola alleviated her symptoms. She had one episode of unconsciousness which occurred one afternoon while shopping. On admission to a local emergency room at that time, she quickly responded to intravenous glucose.

In June of 1969 she was evaluated at another hospital. Repeated blood sugar determinations were in the range of 50 mg%. A 24-hour fasting blood sugar was 40 mg%. An oral glucose tolerance test revealed values consistent with diabetes mellitus with a 3-hour value of 183 mg%, and a 5-hour value of 80 mg%. The fasting blood sugar was 78 mg%. Chest X-ray and intravenous pyelogram were normal. She was treated with a high-protein diet but continued to have two or three attacks per week. She was referred to the diagnostic clinic for further evaluation in August. On physical examination she was a well-nourished lady with normal vital signs. She had a retinal hemorrhage in the left eye, but physical examination otherwise was within normal limits. When originally interviewed one hour after lunch, her responses were rapid and inappropriate; at three hours after lunch her response time lengthened and it often took her seconds to reply to a question. Her responses, however, were appropriate.

Several investigations were carried out to determine the status of her ability to handle a glucose load. A 5-hour glucose tolerance test revealed a flattened curve. The most meaningful values in this test were the fasting blood sugar of 53 mg% and the 5-hour level of 30 mg%. A 24-hour fast was undertaken and blood sugars of 35 mg% and 33 mg% were obtained at 17 and 18 hours respectively. With a blood sugar of 33 mg%, she was unable to do serial 7's and was lethargic. A Tolbutamide tolerance test showed a fasting blood sugar of 53 mg% with a steady decline in blood sugar value until 4 hours after the start of the test when she again became lethargic with a blood sugar level of 23 mg%. Oral leucine-tolerance test was again abnormal with a value of 32 mg%, reached three hours after the administration of 10 grams of leucine.

The patient was operated on on September 2nd, and has had no further symptoms since operation.

DR. LANDSBERG: Dr. Felig will open the discussion.

DR. PHILIP FELIG: Most of us think of islet cell adenomas in terms of Whipple's triad. By this we mean the development of symptomatic hypoglycemia in situations such as caloric restriction or exercise in which there is prompt response to the administration of glucose. This patient's complaints, however, were always post-prandial in timing. Her symptoms occurred between 1:00 and 3:00 in the afternoon. She denied having symptoms in the morning before breakfast. She never complained of hunger, and often had no recollection of any symptoms at all. At times her symptoms were quite specific. She would notice sweating and dullness of her sensorium. Members of her family were more aware than the patient that she was symptomatic and not behaving properly. The family reported that in the afternoon the patient became somewhat bizarre in her affect, slow to respond, and would immediately feel better if fed something with high carbohydrate content. In addition, data obtained at

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the referring hospital revealed a diabetic glucose tolerance test. There was a strong family history of diabetes in that both her parents were affected. Since diabetes is inherited as a recessive trait with perhaps a multifactoral basis, we can assume that she was a genetic prediabetic. There is a strong probability that this patient will ultimately develop diabetes. As many of you know, one of the conditions that can produce hypoglycemia is the early phase of diabetes. Since the patient's symptoms were not apparent in the morning, did not appear to be associated with prolonged fasting, and occurred after food, the question of whether this represented early diabetes was prominent in our minds. There was one fact in her past history which pointed to organic hyperinsulinemia, however, and this was the fact that her blood sugar after a 24-hour fast was 40 mg%, a definitely abnormal finding.

Upon admission to the hospital, it became apparent that she was having evidence of hypoglycemia but was not very attentive to the symptoms. The symptoms of hypoglycemia may be divided into two categories. The first group is related to cerebral hypoxia in that oxygen consumption of the brain is intimately associated with the consumption of glucose. As glucose consumption decreases there is less oxygen consumption and the patient demonstrates evidence of diminished cerebral function. In addition, there is a response on the part of adrenergic nervous system which contributes to the symptoms. The sweating, palpitation, tremor and hunger are manifestations of autonomic dysfunction. The patient was somewhat cognizant of these adrenergic symptoms as she did notice tremor and weakness but she was unaware of the extent to which her intellectual capacities were impaired by the hypoglycemia. We were able to document this during the course of her oral glucose tolerance test and her Tolbutamide tolerance test. Before commencing each of the tests, we had her perform serial 7's. When hypoglycemic, she was unable to handle simple arithmetic. It was of note that after several sets of serial 7's she was able to perseverate and could successfully repeat the sequence of subtracting 7 from 100. However, when asked to do serial 6's she was easily confused.

Another interesting manifestation of her hypoglycemia was hypothermia. We often tend to associate hypothermia with decreased thyroid function. On the basis of our experience with hypothermic patients at Yale, it would appear that hypoglycemia is a far more common cause. Hypoglycemic hypothermia is not necessarily associated with marked depression of the central nervous system but can be seen in patients having only minimal depression of cerebral function. At the present time, we are studying a patient with malignant carcinoid and hypoglycemia who has repeated morning body temperature of 95° or less. A recent study done in the Emergency Room of Yale-New Haven Hospital showed that in 15 consecutive patients admitted to the Emergency Room with hypoglycemia, 50% had body temperatures below 96°.

In considering the various etiologic factors in hypoglycemia, it is reasonable to approach the problem by first looking at the physiologic factors involved in blood glucose homeostasis. One can classify these factors in terms of specific hormones and target tissues that are involved in the regulation of blood sugar. Insulin may be defined as the prime regulatory hormone. Since the other hormones concerned with glucose homeostasis are primarily contra-insulin in their effects, they are referred to as counter-regulatory. (Table 1)

TABLE I

FACTORS IN GLUCOSE HOMEOSTASIS

I. Hormones
    a. Regulatory
        1. Insulin
    b. Counter-regulatory
        1. Epinepherine
        2. Glucagon
        3. Cortisol
        4. Growth Hormone
II. Tissues
    a. Liver
        1. Glycogenolysis
        2. Gluconeogenesis
    b. ? Neoplastic Tissue
        1. ? Glucose overutilization

The function of insulin must be considered not only in terms of increasing peripheral tissue glucose utilization, but also in terms of the effects of insulin on the liver. Insulin is secreted directly into the portal circulation. Since the liver is the prime site for insulin degradation, insulin may have effects on the liver without apparent effect on peripheral glucose utilization. With respect to glucose homeostasis, insulin has a dual effect on the liver. 1) It stimulates the enzyme, glycogen synthetase, resulting in increased extraction of glucose from the portal circulation and increased glycogen deposition in the liver. 2) It inhibits gluconeogenesis. Insulin will prevent the formation of glucose from non-glucose substrates, both those coming from protein in the form of amino acids and those derived by recycling of glycolytic intermediates such as lactate and pyruvate. Insulin has a three-fold effect in terms of lowering blood glucose. It increases glucose utilization peripherally and has a dual effect on the liver. This regulatory role of insulin pertains in situations of caloric intake as well as deprivation. Although we think of insulin in terms of a response to oral or parenteral glucose or other stimuli in which the blood glucose tends to rise, in fasting, the maintenance of a normal blood sugar is contingent upon a diminution of insulin secretion. There is a very tight feedback regulation in which a hyperglycemic situation results in stimulation of insulin secretion, while a lack of glucose or lack of caloric intake is accompanied by a diminution in insulin secretion. This is the physiologic basis of a prolonged fast in diagnosing insulinoma.

With respect to the counter-regulatory hormones, the effects of epinephrine are well-known in terms of stimulation of glycogenolysis and gluconeogenesis, and inhibition of peripheral glucose utilization. This latter aspect is not as well-recognized but there is evidence, particularly in terms of the beta effect, that stimulation of beta receptors results in diminished utilization of glucose. Glucagon has a similar effect in terms of stimulating gluconeogenesis and glycogenolysis but does not have the effects in terms of peripheral utilization. With regard to cortisol, we are dealing primarily with its effect on mobilization of precursors for gluconeogenesis in the form of amino acids, an action which relates to the catabolic role of glucocorticoids. In addition, cortisol may have an anti-insulin type of effect on glucose uptake. Finally, growth hormone is important in terms of glucose homeostasis. Its anti-insulin effect is evident from the fact that growth hormone causes less of a blood glucose fall for any given amount of insulin. In addition, growth hormone is important in stimulating lypolysis which may provide additional substrate for gluconeogenesis in the form of glycerol. It should be remembered that fat is stored in the form of triglycerides. In breaking down fat, we are releasing not only fatty acids, but also glycerol, which can be used for gluconeogenesis.

In considering the target organs involved in the regulation of blood glucose, the liver is the primary tissue of importance. However, there may be clinical situations where neoplastic tissue is important in blood glucose regulation. Various tumors produce hypoglycemia in the absence of hyperinsulinemia by causing over-utilization of glucose.

For the clinician, it is important to have a classification of hypoglycemia that can be related to the patient's symptoms and which will permit a logical approach to the problem of diagnosis. The various physiologic mechanisms discussed above may be helpful in understanding why specific tests are useful, but for the physician faced with the patient at the bedside, it is important to have a classification that will permit ready application of the clinical findings. Rather than classify hypoglycemia in terms of over-utilization or under-production of glucose as has been the tendency in the past, I think it is of better use to the clinician to think in terms of three categories: 1) post-prandial; 2) fasting; and 3) induced hypoglycemia. (Table 2)

TABLE 2

CLASSIFICATION OF HYPOGLYCEMIA

I. Post prandial
    1. Alimentary (gastrectomy, gastroenterostomy).
    2. Functional, Reactive
    3. Early Diabetes
    4. Genetic Dietary Intolerance (fructose, galactose, leucine)
II. Fasting
    1. Hepatic Disease (congenital, acquired)
    2. Adrenal Insufficiency
    3. Pituitary Insufficiency
    4. Insulinoma
    5. Non-beta cell tumors
III. Induced
    1. Alcohol
    2. Hypoglycin
    3. Exogenous insulin, sulfonylureas

The post-prandial hypoglycemias are those types of hypoglycemia which would not occur in situations in which there is no caloric intake. In this group, with the possible exception of patients with leucine intolerance, there would be no circumstance where we would anticipate hypoglycemia in the fasting state. In post-prandial hypoglycemia, there must be the interposition of some type of stimulus in the form of food ingestion to produce hypoglycemia. Examples of post-prandial hypoglycemia are seen in patients who have undergone subtotal gastrectomy or gastoenteroscopy and developed symptoms of hypoglycemia about two hours after a meal. It has been postulated that the rapid entry of glucose into the upper bowel allows for more rapid absorption than one is normally accustomed to and a resultant excessive rise in blood sugar. This results in an exuberant insulin release on the part of the pancreas. Another situation in which we see post-prandial hypoglycemia is in patients with functional or reactive hypoglycemia. This may well be the most common type of hypoglycemia that one encounters. It is a situation often seen in women from 30 to 40 years of age who tend to be somewhat tense and anxious and who complain of symptoms of lightheadedness, headache, and confusion, occurring from 3 to 5 hours after meals, but never in a situation where they have not eaten. Initially, we thought our patient might fit this picture because of the timing of her symptoms. The mechanism of hypoglycemia in these individuals is not entirely understood. In some studies a hyperinsulinemic response has been demonstrated while in other patients there is no increase in insulin and one cannot really account for the decrease in blood sugar. There is the impression that in functional hypoglycemia one does not get as profound a fall in blood glucose as one sees in the organic or fasting types of hypoglycemia, but there are a fair number of documented instances of functional hypoglycemia with blood sugars as low as 25 mg%. I don't believe it is possible to use the magnitude of decrease in blood sugar as a definite diagnostic point. Another interesting clinical point about functional hypoglycemia is that this condition has been recognized with greater frequency in recent years in patients with peptic ulcer disease. This may have same physiologic counterpart in that it has become apparent in the last few years that insulin secretion in part depends upon gastointestinal secretagoges, such as secretin, gastrin, and pancreozymin. Recent studies indicate that with the ingestion of glucose there is an increase in serum secretion to levels which are known to be capable of stimulating insulin secretion in peptic ulcer disease. Since hydrochloric acid upon its entry into the duodenum is the most potent stimulus to secretin secretion, it is possible that the hyperacidity of peptic ulcer disease results in a hyperinsulinemic response to glucose on the basis of this gastrointestinal hormonal imbalance. This might correlate with the fact that as many as 50% of patients with peptic ulcer disease have been found to have evidence of functional hypoglycemia. The third type of post-prandial hypoglycemia is the early diabetic phase, which we mentioned before. In this circumstance, one is dealing with a very marked increase in blood sugar early in a glucose tolerance test. There is a sluggish outpouring of insulin initially following a glucose load but ultimately a marked increase in serum insulin. This results generally in an abnormally high peak blood glucose level in the first one to two hours followed by an abnormally low glucose level at three to four hours.

A group of conditions not often seen in adult patients are the genetic dietary intolerances, wherein various substances cannot be handled because enzymatic deficiencies cause a disturbance in blood glucose homeostasis. Examples of this type of condition include fructose and galactose intolerance. In the case of fructose intolerance there is an inhibition of gluconeogenesis presumably because of accumulation of fructose-1-phosphate. In cases of galactosemia, hypoglycemia during milk ingestion is not unusual. Accumulation of galactose-1-phosphate apparently interferes with hepatic glucose uptake. With leucine intolerance in children, one is dealing generally with a hypersensitive islet cell response to the insulinogenic stimulus of leucine.

The fasting types of hypoglycemia are commonly referred to as organic hypoglycemias. In this category, symptoms classically develop in fasting situations. Hepatic disease is an example of this type. This can be easily understood in view of the gluconeogenetic and glycogenelytic capacity of the liver in glucose homeostasis. Clinically, however, hypoglycemia in liver disease has been considered to be restricted to instances of severe diffuse hepatic damage. Recently, we have been interested in several patients hospitalized at Yale with viral hepatitis. Several of these patients with hepatitis, many of whom were only mildly ill and had been eating well, had blood glucoses below 50 mg%, with blunted responses to glucagon. Hypoglycemia may be more common in hepatitis than formerly realized.

In adrenal insufficiency, it has long been recognized that hypoglycemia may be prominent manifestation of the disease, although it is usually the electrolyte abnormalities which produce the signs and symptoms which lead the patient to consult his physician. There is, however, a form of adrenal insufficiency in which hypoglycemia may be the paramount if not the sole problem. I am speaking of isolated ACTH deficiency. In this condition, one sees neither the mineralocorticoid deficiency nor the hyperpigmentation characteristic of spontaneous Addison's disease. Unexplained hypoglycemia or a particular sensitivity to alcohol hypoglycemia is often the presenting complaint. In dealing with a hypoglycemic patient, the presence of normal electrolytes and the fact that the patient does not have orthostatic hypotension or hyperpigmentation does not eliminate the possibility that one is dealing with an organic type of hypoglycemia caused by an isolated deficiency of ACTH. To rule out this diagnosis, it is necessary to determine urine hydroxy-corticoids or plasma cortisol levels.

Functioning islet cell tumors of the pancreas or insulinomas are a most important form of hypoglycemia, because in over 70% of cases they are curable. These tumors are generally benign. In 20%-30% of cases the tumors may be multiple or malignant. Characteristically, patients with insulinomas complain of hunger and are most likely to be symptomatic in the morning. However, this is not always the case as was so clearly seen in the patient presented today. Her symptoms were restricted to the early afternoon. As will be shown later, this was due to the autonomous function of her tumor which tended to secrete increased amounts of insulin in the early afternoon regardless of the patient's caloric intake.

Other tumors associated with hypoglycemia are predominantly of mesodermal origin, such as mesothelioma, fibrosarcoma, lipomas or neuromas. These tumors are often quite large and located in the retroperitoneal space or mediastinum. They may present clinically with hypoglycemia, but the physician is aided by the fact that palpable masses are often felt due to the large tumor bulk. Other tumors of non-mesodermal origin associated with hypoglycemia include primary hepatic tumors, an occasional gastric carcinoma, cecal carcinomas, and, as mentioned previously, carcinoid tumors.

The third group of hypoglycemic syndromes is the induced group. In a sense, this group is similar to post-prandial hypoglycemia in that it depends upon the interposition of some substance for the development of hypoglycemia. In this group we are not dealing with the ingestion of food or protein but rather with the ingestion of some medication or alcohol. Alcohol hypoglycemia generally occurs in malnourished individuals. In this situation fasting hypoglycemia develops in a person who has been predisposed to the development of alcohol hypoglycemia by the depletion of glycogen stores. Alcohol presumably interferes with gluconeogenic mechanisms related to change in the redox conditions in the liver. As alcohol is being oxidized, there is an increase in reduced forms of co-factors, namely DPN. There is a diminution of the ratio of DPN to DPNH which in turn inhibits gluconeogenic mechanisms. For this defect in gluconeogenesis to become manifest clinically, it is necessary to have a situation in which glycogen deposits have been dissipated. Therefore, we see this condition only in malnourished individuals such as alcoholics who have been drinking heavily without adequate caloric intake.

A second form of induced hypoglycemia is that caused by hypoglycin, which is a derivative of the West Indian ackee nut. Compounds present in the ackee nut interfere with fatty acid utilization which in turn inhibits gluconeogenesis. This is another situation in which a drug produces hypoglycemia.

The most common form of induced hypoglycemia which we encounter is the result of exogenous insulin administration or secondary to sulfonylurea administration.

TABLE 3

DIAGNOSTIC STUDIES IN HYPOGLYCEMIA

1. Overnight fasting blood glucose and serum insulin (X3)
2. Oral glucose tolerance test (5 hours).
3. Tolbutamide tolerance test (blood glucose >40).
4. Leucine tolerance test.
5. Blood glucose and serum insulin response to prolonged (18-72 hours) fasting.

The diagnostic studies which we can use in approaching a patient with hypoglycemia are shown in Table 3. If one is concerned with an islet cell tumor, obtaining three fasting blood sugars and simultaneous serum immunoreactive insulins can be the quickest way to make the diagnosis. If one can demonstrate in the overnight fast, a decrease in blood sugar below 50 mg% accompanied by an increased or normal level of insulin, the diagnosis of islet cell tumor is indicated. If serum insulin levels are low or undetectable, one could still be dealing with organic hypoglycemia consequent to a non-islet cell tumor. When a patient describes symptoms suggestive of hypoglycemia and it is not clear if these symptoms are occurring in the fasting or post-prandial state and overnight fasting blood glucose is normal, the oral glucose tolerance tests may be helpful. If one is dealing with a reactive type of hypoglycemia, the symptoms of hypoglycemia may be brought out by the interposition of a glucose stimulus. In this situation, we would expect a fall in blood glucose about three hours after the administration of glucose. The blood sugar should then return to normal. If neither of the above tests provides a diagnosis, the next step is the Tolbutamide tolerance test. If one is considering the diagnosis of islet cell adenoma, it is imperative that the fasting blood sugar be known before the administration of Tolbutamide. Tolbutamide should never be given when the blood sugar is below 40 mg%. The basis for this precaution is the possible induction by Tolbutamide of profound hypoglycemia, which may persist for 12-24 hours, when the blood glucose level is 40 mg% or less at the start of the test. This carries the potential danger of irreversible cerebral damage. The use of Dextrostix makes it possible for the fasting sugar to be determined at the bedside during the test with a syringe filled with 50% glucose readily at hand. If symptoms develop, the diagnosis is made. Blood for glucose determination should be immediately drawn and dextrose administered. Normal individuals do not exhibit a profound drop in blood sugar. In some patients with islet cell tumors, there is no response to Tolbutamide. In these cases, leucine tolerance tests can be helpful. Amino acids can stimulate insulin secretion and in individuals with islet cell tumors there is an increased sensitivity to the insulinogenic capacity of amino acids, particularly leucine. In 60-70% of patients with islet cell tumors, one observes a decrease in blood sugar and an exuberant insulin response following leucine ingestion. If the above tests are not helpful, then one should study the response of blood sugar and insulin to a prolonged fast. In the case presented today, this was the definitive study.

In our patient, several fasting simultaneous blood sugar and insulin levels failed to demonstrate hypoglycemia, with the exception of one value of 53 mg% which may be considered borderline. All serum insulins were normal. We then turned our attention to the glucose tolerance test. This test revealed a marked fall in blood sugar 4 hours after glucose administration; however, there was no corresponding rise in serum insulin. The initial glucose values are in the diabetic range with a blood sugar of 120 mg. % at two hours. In this study we saw no response of insulin secretion to glucose administration. This explains why we can have a diabetic type of glucose tolerance test in a patient with an insulinoma. In normal individuals with normal pancreatic tissue, glucose is the most profound stimulus for insulin secretion; in neoplastic islet cell tissues there is often a lack of response to glucose. In this patient, although the blood sugar response did not improve very much following surgery, post-operative insulin levels demonstrated that the remaining one-third of her pancreas was now able to respond appropriately to a glucose challenge. (Tables 4 and 5)

The Tolbutamide tolerance test should be looked at, both in relation to the fall in blood sugar and the length of time the blood sugar remains low. In normal individuals, the blood sugar falls slightly and then reverts to normal. In patients with insulinoma, there is a more profound and precipitous fall and the blood sugar remains low. In addition, one sees an increased serum insulin level, although this is not a uniform finding. In our patient, the administration of Tolbutamide led to a fall in blood sugar but no corresponding increase in serum insulin. The fall in blood sugar which we observed at 2½ hours following Tolbutamide might have occurred without the Tolbutamide and did not represent a response to the drug. Our data indicates that post-operatively, the patient had a greater insulin response to Tolbutamide than before surgery. (Table 6)

The leucine tolerance test did show a fall in blood glucose and corresponding increase in levels of serum insulin. Post-operatively, the administration of leucine did not produce a fall in blood sugar or increase in serum insulin. (Table 7)

It is of interest that the responsiveness of an islet cell tumor is unusual. In general, we speak of neoplastic tissue as being primitive tissue. The neoplastic islet, or insulinoma, is really very much like

TABLE 4

FASTING BLOOD SUGAR AND INSULIN LEVELS IN PATIENT C.V.

Date	*Glucose*	*Insulin*
8/25	59, 53	<10, 11
8/26	53, 59	13, <10
8/27	65	14
8/28	75, 64	14, 14
		Normal (<30)

TABLE 5

PRE-OPERATION

8-25-69

5 HR. ORAL GLUCOSE TOLERANCE TEST

Time	*Glucose mg%*	*Insulin μU/ml*
—10	59	<10
0	53	11
30	104	<10
60	132	<10
90	106	14
120	120	12
180	110	60
240	48	14
300	30	26

POST-OPERATION

9-29-69

5 HR. ORAL GLUCOSE TOLERANCE TEST

Time	*Glucose mg%*	*Insulin μU/ml*
—60		<10
—30	88	<10
+30	116	47
+60	109	28
+90	110	26
+120	119	79
+180	90	62
+240	93	17.5
+300	64	<10

the fetal or neonatal pancreas. In premature infants following a glucose stimulus, blood glucose rises but there is almost no response to insulin. Following amino acid infusion, there is a marked increase in insulin. In the developing pancreas, therefore, there is more response to amino acids than to glucose. This situation is seen in the patient's islet cell adenoma.

As noted previously, insulin is of importance not only in terms of lowering the blood glucose following carbohydrate administration but it is also important in maintaining the blood sugar when one is deprived of carbohydrate. In normal individuals during the course of a prolonged fast, there is a fall in serum insulin. In almost all instances, the fasting insulin level will fall to less than 15 micro units per ml (provided the individual is not obese). In addition, the blood glucose will remain above 50 mg% and no symptoms of hypoglycemia will develop. In our patient we did not see this. In response to an 18-hour fast, a progressive fall in blood glucose and corresponding rise in serum insulin was observed. This was the hallmark of this patient's organic hypoglycemia. One month post-operatively, when restudied, she had no fall in blood sugar and her insulin remained quite low during a similar period of fasting. We can therefore characterize the hypoglycemia in our patient as being due to autonomous insulin secretion for there was no cessation of insulin secretion with fasting such as is seen in normal individuals. This autonomy or continued secretion of insulin in a situation where one should not see hyperinsulinemia pointed to the diagnosis of islet cell adenoma. (Table 8)

TABLE 6

PRE-OPERATION
8-26-69
TOLBUTAMIDE TOLERANCE TEST

Time	*Glucose mg%*	*Insulin μU/ml*
—10	53	12.5
0	59	<10
+10	53	34.5
20	48	16
30	45	13
40	43	14
60	41	14
75	39	22
90	36	13
120	30	27
180	23	22

POST-OPERATION
9-30-69
TOLBUTAMIDE TOLERANCE TEST

Time	*Glucose mg%*	*Insulin μU/ml*
—10	85	<10
0	84	<10
15	67	90
30	43	16
45		<10
60	63	<10
90	67	<10
120	64	<10
150	71	<10
180	68	<10

Occasionally we see metastatic islet cell tumors

TABLE 7

PRE-OPERATION
8-28-69
ORAL LEUCINE TOLERANCE TEST

Time	*Glucose mg%*	*Insulin μU/ml*
—10	75	14
0	64	14
15	67	33
30	59	48
45	55	60
60	47	38
90	40	33
120	35	34
180	32	32

POST-OPERATION
10-1-69
ORAL LEUCINE TOLERANCE TEST

Time	*Glucose mg%*	*Insulin μU/ml*
—15	87	<10
0	90	<10
+15	90	10
30	90	14
45	84	17
60	79	17.5
90	74	<10
120	76	<10
180	76	<10
240	79	<10

TABLE 8

PRE-OPERATION
8-27-69
PROLONGED FAST

Time	*Glucose mg%*	*Insulin μU/ml*
13 hr.	65	14
17 hr.	35	39
18 hr.	33	27

POST-OPERATION
PROLONGED FAST
10-2-69

Time	*Glucose mg%*	*Insulin μU/ml*
13 hr.	93	<10
14 hr.	92	no sample
16 hr.	93	<10
19 hr.	87	<10

in which surgical intervention would not be helpful. In that circumstance there are two new drugs which have become available. One of these is Diazoxide, a drug which is related chemically to the benzothiadiazine diuretics and which has recently been recommended for use in the intravenous form in hypertensive encephalopathy. This drug acts by inhibiting pancreatic insulin secretion both in normal islet tissue and in adenomatous tissue. The drug may also have a role in directly decreasing peripheral glucose utilization. However, in contrast to the thiazide diuretics, Diazoxide may cause sodium retention resulting in peripheral edema. A new drug recently made available is Streptozotocin, an antibiotic derived from a species of streptomyces. This drug has a specific effect in destroying the islet cell tissue in the way similar to that of alloxin. However, it is less toxic and more predictable in its effects than alloxin.

DR. LEWIS LANDSBERG: Dr. Goldenberg operated on this lady, and will discuss the surgical aspects of her problem.

DR. IRA S. GOLDENBERG: From the clinical history it was reasonable to presume that this patient had hyperfunction of her insulin producing apparatus, most likely an islet cell adenoma. When facing this problem, one must recognize that he may be dealing with a very small tumor. We hoped to obtain some information from celiac angiography and radio selenium scan of the pancreas, but these studies were not helpful. At the time of exploration, it was immediately apparent that we were not dealing with a large tumor. A significant percentage of these patients present with several tumors which may create a problem, since finding one tumor does not preclude the presence of additional ones. Most of the tumors, whether single or multiple, appear in the body or tail of the pancreas, so that it is possible to palpate and visualize with ease the portion of the gland most often involved. Some patients have tumors in the head of the pancreas, however, which presents a more difficult challenge because it is difficult to mobilize this portion of the pancreas and adequately evaluate it. One or two percent of patients with insulinomas have aberrant pancreatic tissue which contains the adenoma. The most common extra-pancreatic site is near the splenic pedicle. Other sites include the stomach wall and, on rare occasions, the wall of the small bowel. In this patient we were able to mobilize the pancreas quite adequately, yet were unable to find any tumor. The possibility existed that we were dealing with diffuse hyperplasia rather than with an adenoma, since this does occur in a small percentage of cases but seemed unlikely with such a normal-appearing organ. We nonetheless elected to do a subtotal pancreatectomy. The body and tail of the pancreas were mobilized and the gland was reflected upwards, at which point we noticed a tiny nodule about 1 cm. × 1 cm. posteriorly in the head of the pancreas which looked like an adenoma. The nodule was easily excised and frozen section confirmed the impression that this was an adenoma. The subtotal pancreatectomy was completed and a 4 × 4 cm. remnant of the head of the pancreas was left *in situ*. The patient's post-operative course was uneventful and she was discharged from the hospital ten days after operation.

DR. SAMUEL KUSHLAN: Was the remainder of the pancreas normal?

DR. GOLDENBERG: Yes.

DR. THOMAS AMATRUDA: Why was a subtotal pancreatectomy performed when the insulinoma was found?

DR. GOLDENBERG: Because previous to its discovery we had committed ourselves to resection and, for technical reasons, the mobilized portion of the pancreas had to be excised.

A PHYSICIAN: Many of us have eliminated the Tolbutamide tolerance test from our diagnostic protocol because we have seen normal patients who have reached markedly hypoglycemic levels and patients with documented islet cell adenomas who had normal Tolbutamide tests. Would it not be better to use the fasting insulin level and if this is not diagnostic, follow that up with a prolonged fast?

DR. FELIG: I think the virtue of the Tolbutamide tolerance test would be in a situation in which one is unable to demonstrate a low blood glucose within 18 hours or so of fasting. It is often hard to convince a patient to go through with a 72 hour period of fasting. In this circumstance the Tolbutamide tolerance test might be helpful. I think you are quite right, however, in that about 30% of patients with islet cell adenomas have no response to Tolbutamide.

A PHYSICIAN: How do you explain the post-prandial timing of the symptoms?

DR. FELIG: I think we are dealing primarily with a spontaneous secretion of insulin in an inattentive patient who may have had milder symptoms in the morning as well but was not attuned to it. Perhaps she was eating more protein at lunch and in view of her leucine sensitivity, this might also help to explain the post-prandial symptoms.

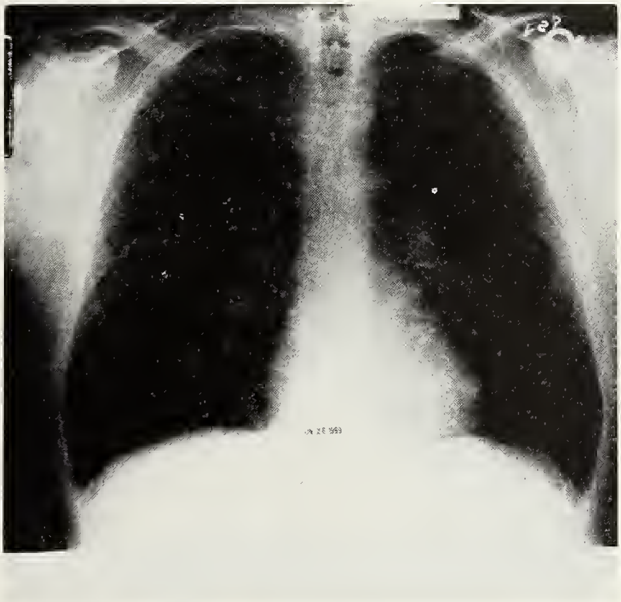
X-Ray of the Month

Section of Chest Diseases

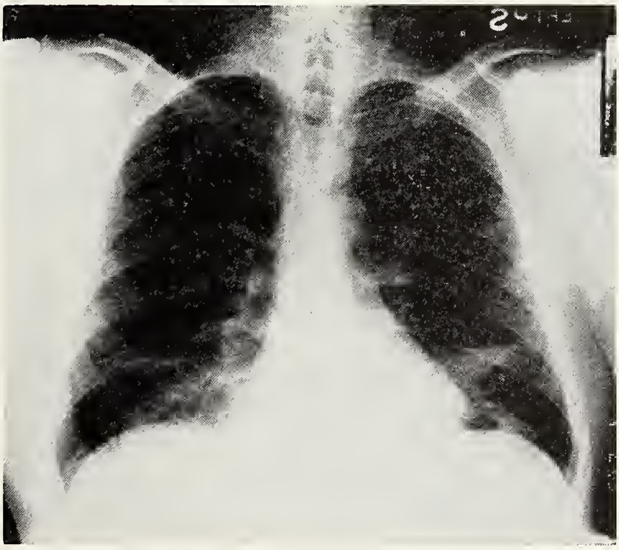
Arnold B. Rilance, M.D., Director, Winchester Chest Clinics

History

F.G., #75-43-20, a 43 year old postal clerk, was admitted to the Yale-New Haven Hospital on 6/29/69. *Chief Complaint*: The sudden onset on awakening of breathlessness and exertional dyspnea, provoked by climbing stairs and attempting to mow the lawn. The same afternoon, while scuba diving, he became very short of breath. There was no chest pain, skeletal pains or neurological symptoms.



Admission X-ray of chest revealing normal lung fields without infiltration.



Conventional X-ray of chest 4 days later reveals bilateral basilar infiltration with some changes suggestive of lobular atalectasis.

Physical Examination

Dusky, tachypneac; B.P.-130/80; P.-130; R.-30; T.-102°. Chest: distant breath sounds. No wheezing. Some moist rales were heard bilaterally.

Arterial Blood Gases:

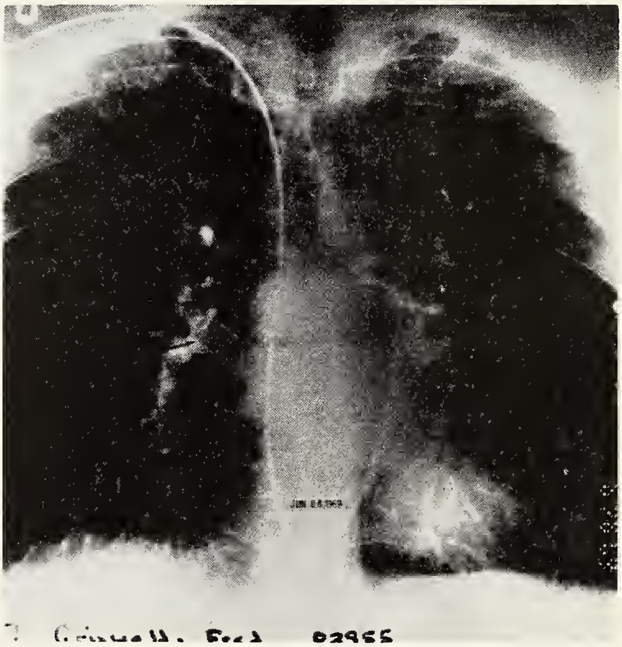
Room Air:	PO_2-48	PCO_2-24
10 L. O_2/min.	PO_2-70	PCO_2-26

Course

Seven hours following admission, the patient was much less dyspneac. Temperature: 98.6. He had, however, a severe headache and a lumbar puncture was performed, which was normal.

A pulmonary arteriogram on admission was read as inconclusive.

A lung scan performed subsequently demonstrated a large perfusion defect in the lower right



Pulmonary arteriogram demonstrating diffuse impairment of perfusion. Arrows point to large defects in main pulmonary arteries due to thrombi.

lung field, with smaller defects in the left lower lung field. He was started on Heparin therapy.

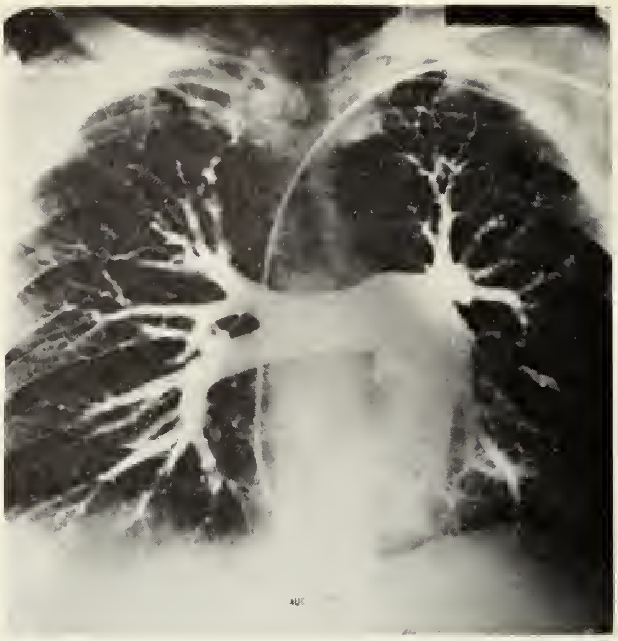
A repeat arteriogram five days later revealed normal perfusion of the major pulmonary arteries with cut-off of several small vessels.

Diagnosis

Embolization of both major pulmonary arteries.

Discussion

This case presents a classical history of pulmonary embolism of the major pulmonary arteries. Physical findings were not remarkable. The initial X-ray shows no abnormality. The low arterial blood O_2 saturation in the presence of a low PCO_2 is also quite characteristic. A high index of suspicion, resulting in studies such as a lung scan and pulmonary arteriography, is important in leading to a correct diagnosis.



Repeat pulmonary arteriogram showing improved perfusion with only minor changes due to small vessel occlusion.

Members of the Connecticut State Medical Society reading papers before other organizations are requested to submit their papers to the JOURNAL for consideration by the Board of Editors for publication. Please send them to:

Louis H. Nahum, M.D., *Editor*
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51270G

Electrocardiogram of the Month

Yale-New Haven Hospital
New Haven, Connecticut
Prepared by
HYMAN M. CHERNOFF, M.D.
Associate Professor of Clinical Medicine,
Yale School of Medicine
Director, Dept. of Electrocardiography
Memorial Unit, Yale-New Haven Hospital

Therapeutic considerations often make it necessary to clearly differentiate between so-called true ventricular extrasystoles and ventricular ectopic beats which arise in a parasystolic focus. In the case of true ventricular extrasystoles it is assumed that the extrasystole is in someway dependent upon or precipitated by the preceding sinus beat since such beats usually exhibit constant coupling intervals with the preceding sinus beats. This is the usual finding when digitalis excess results in periods of bigeminal rhythm and is an indication for stopping the drug. In ventricular parasystole, however, the parasystolic center from which ectopic impulses arise is not influenced by the spread of the sinus impulse and therefore the ectopic beats do not exhibit constant coupling intervals with the preceding sinus beats. In addition since such parasystolic centers emit impulses quite regularly the interectopic intervals will be quite constant with the longest interectopic intervals being an exact or nearly exact multiple of the shortest. Should the ectopic focus discharge happen to fall in the absolute re-

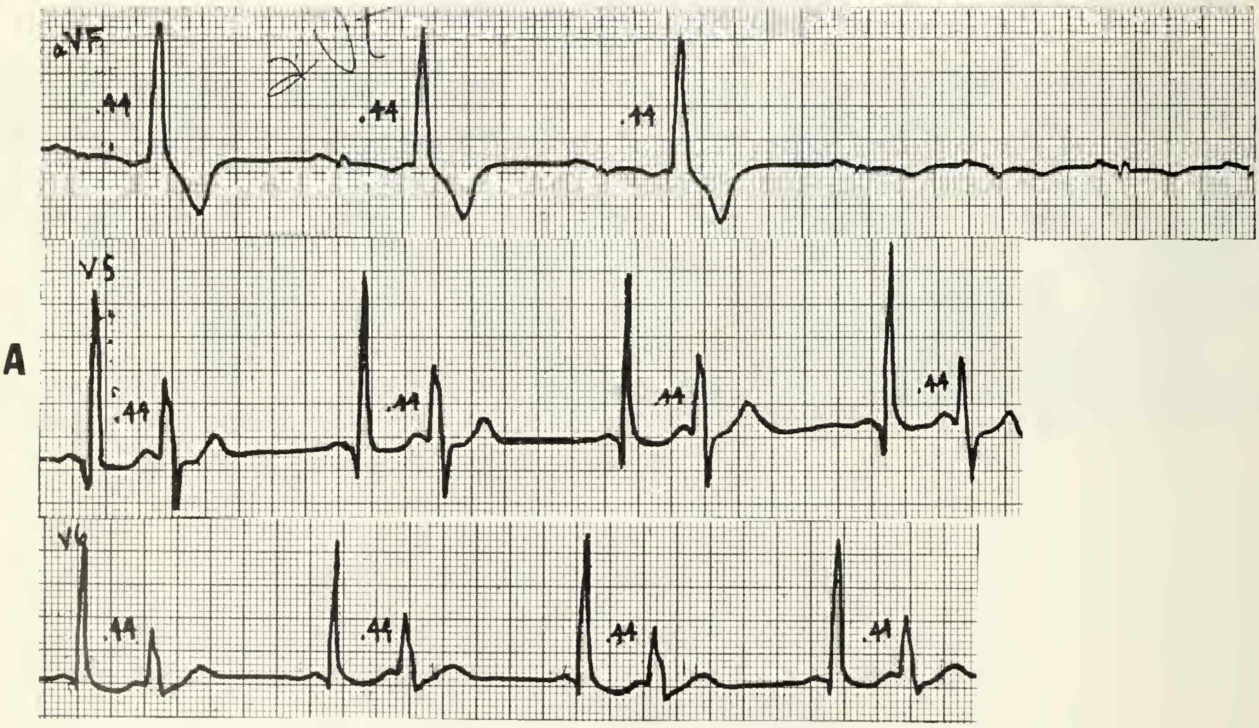


Figure A

These leads were obtained in a patient with a recent inferior wall infarction after receiving an excess amount of digitalis. All of the ventricular extrasystoles exhibit identical coupling intervals (.44 sec.) with the preceding sinus beats. The extrasystoles subsided about 36 hours after withdrawal of the digitalis.

fractory period following a normal sinus beat it will fail to elicit a ventricular response. At times the discharge of the parasystolic focus will coincide with the passage of the sinus impulse through the ventricles giving rise to fusion beats. If the above three criteria are found in a tracing the diagnosis of parasystole can be made with certainty. Since ventricular parasystole is rarely a manifestation of digitalis excess and is usually an indication of organic heart disease, its presence is therefore not a contraindication for instituting or continuing digitalis therapy.

Below are two tracings from different patients illustrative of true ventricular extrasystoles and ventricular parasystoles.

B

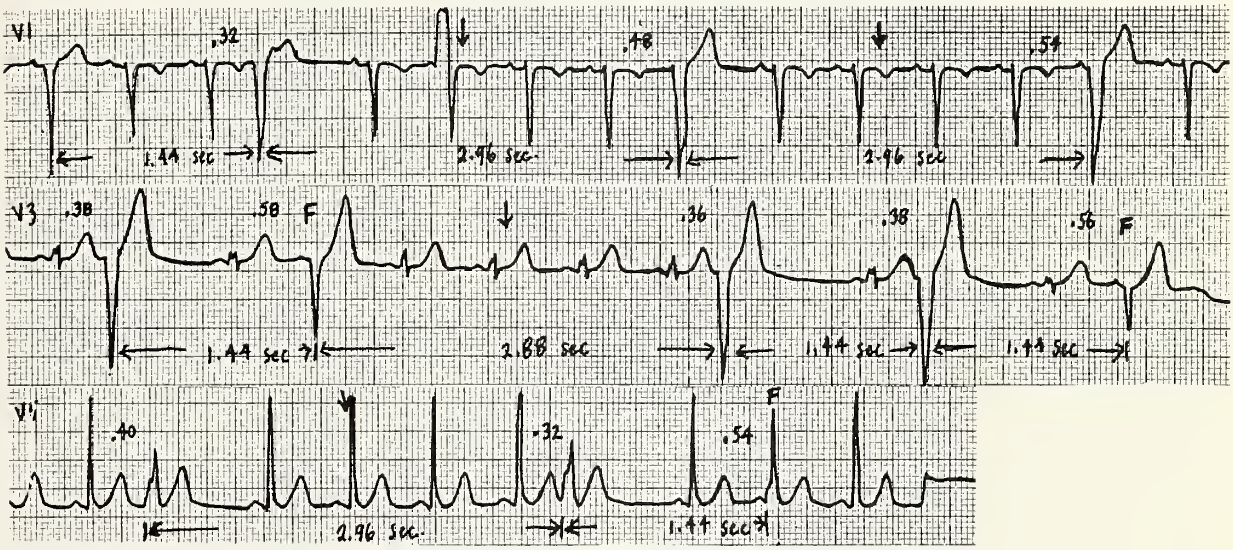


Figure B

These leads were obtained in a patient with arteriosclerotic heart disease in acute congestive failure. The ventricular ectopic beats exhibit varying coupling intervals to the preceding sinus beats, ranging from 0.32 sec. to 0.58 sec. The shortest interectopic interval measures 1.44 sec. (there are 5 such intervals in the 3 leads shown). The longest interectopic intervals measure 2.88 sec. and 2.96 sec. (an exact and nearly exact multiple of 1.44 sec.). Arrows indicate where an expected parasystolic beat fails to elicit a ventricular beat because of its falling in the absolute refractory period of the sinus beat. On two occasions when the parasystolic beat falls shortly after the inscription of a sinus P-wave, fusion beats (labelled F) are noted. The basic interectopic interval of 1.44 sec. suggests a parasystolic rate of about 42/min. The arrhythmia subsided after full digitalization and improvement in cardiac function.

By The London Post

British National Health Services

Part III

Ned Thomas

(This is the third of a series of six articles)

LONDON, England—Even if the Conservative Party of the late Winston Churchill were to win control of the government from the Labour Party tomorrow, it would certainly retain the National Health Service, which Americans call socialized medicine. The service provides free, comprehensive medical and health care for practically everyone in the country.

This was made unmistakably clear in an interview with Conservative Member of Parliament Maurice Macmillan who is the official Tory spokesman on health matters and who would become the next Minister of Health should the Tories become the dominant force in the government.

In fact, at the Conservative Party's recent convention held at Brighton, its leader, Mr. Edward Heath, who would become the Prime Minister if the Tories are returned to power in the next British general election, did not include the National Health Service as an issue that the party would put before the public in an attempt to win its support.

Instead, the issues he singled out were immigration, law and order, and Rhodesia. These, he insisted, were the issues that the party should concentrate on.

Mr. Maurice Macmillan, son of former British Prime Minister who served in that capacity from January, 1957, to October, 1963, gave the following answers to our questions:

Q. Is the National Health Service here to stay?

A. Yes it is. Obviously! There's no doubt about that!

Q. Then the Conservative Party is firmly committed to it?

A. Yes, the Tory Party has been committed to it since 1945. The (late Lord) Beveridge report was introduced during the war and supported by all parties. (Lord Beveridge was a prominent member of the Conservative Party and served in the wartime cabinet of the late Prime Minister Churchill.)

Q. Then the Conservative Party would not ask for the repeal or abolishment of the National Health Service?

A. It is not a thing that we can repeal or abolish. It's a system that has developed over the years and (has been) changing. We shall modify it to some extent and try to find methods, just as this (Labour Party) Government has done, of running it better and more smoothly, and financing it, perhaps, slightly differently. In general, (we would) assist and develop it in a way that is suitable for the modern world.

Q. Do you think the way it is being run now is bad, or that it should be modified considerably?

A. We have made absolutely certain that everyone in the country—no matter how rich or how poor—gets exactly the treatment they need. We do need considerable improvements in the standards of care of the chronically sick—particularly improvement of the hospital service to avoid so much waiting, better conditions for doctors—both hospital and general practitioners, and better paying conditions for nurses.

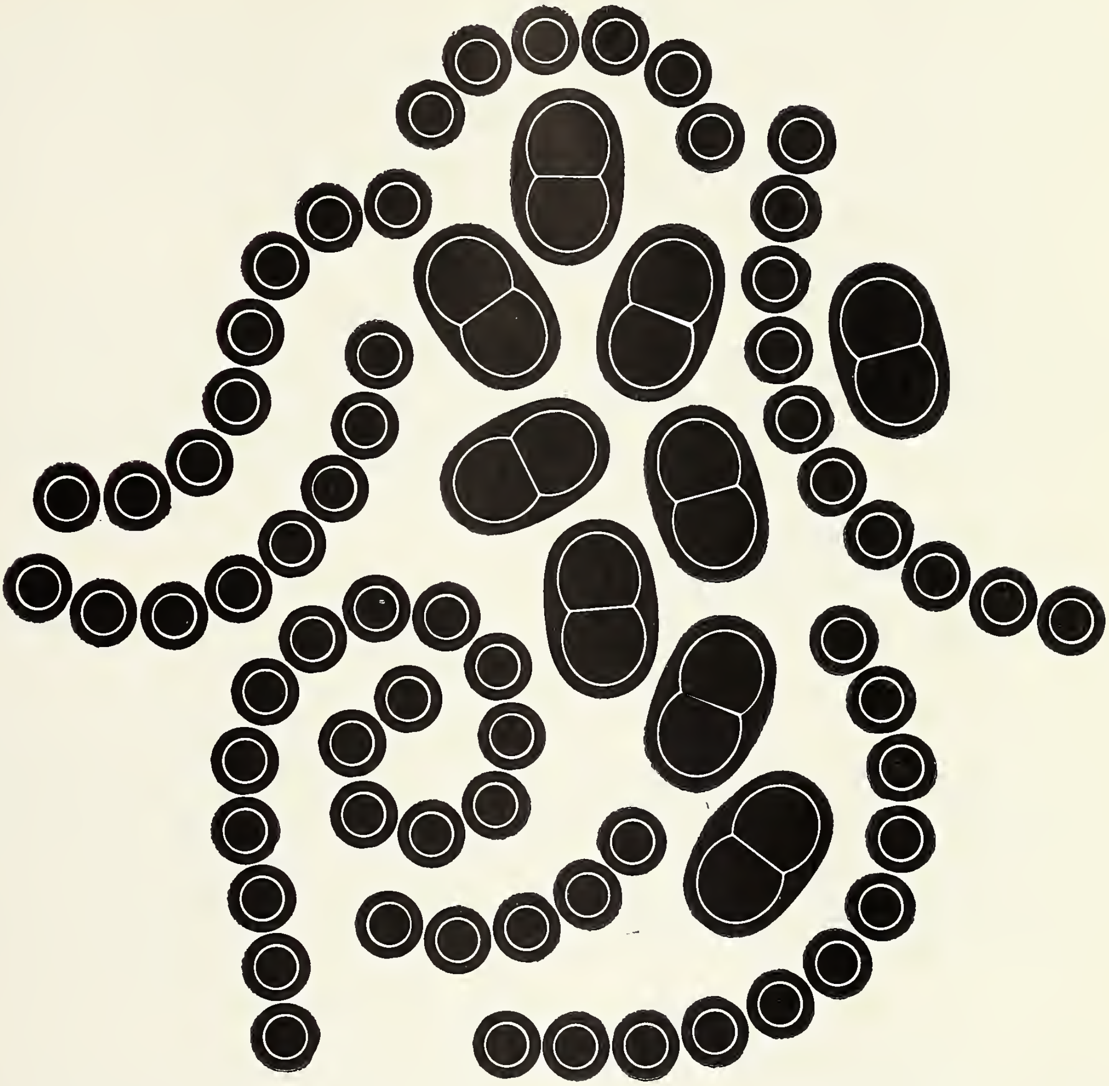
There is a need to reduce some of the general practitioners' lists (which consist of the number of patients individual G.P.'s treat) to enable them to operate more effectively. Also, they need better equipment and better premises. Certain adjustments have to made in the hospital doctor system, but these are all part of a developing program to meet new needs.

(In a recent speech Mr. Macmillan gave, he said: ". . . it has been obvious for some time that changes in the administrative structure will not solve the main dilemma facing the National Health Service, which is at the moment virtually one of rationing. Demand is almost unlimited; resources, both in terms of man-power and money, are very limited.

("At the moment, the gap is filled by increasing

MR. NED THOMAS is a science medical writer for the New Haven Register on leave.

during and after infection



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delay in non-urgent medical care and increasing frustration among those who provide it in increasingly unsatisfactory conditions. Rationing is by the queue.")

Q. Is the National Health Service costing too much for what it is giving?

A. It does not get enough of the gross national product (which is the sum total of all the goods and services produced annually in England). We don't spend as much proportionately on health care as do Canada or the United States.

England spends about 5¼ per cent of its gross national product on its National Health Service, whereas the U.S. spends more than 6 per cent of its gross national product on health.

(In his speech Mr. Macmillan said: "According to the Government's own figures, in 1967-68 the figure was 1,662 million (English pounds or almost $4 billion American dollars); in 1968-69, it has risen to 1,785 million (English pounds or almost $4.3 billion); and in 1969-70 it will be a total of 1,876 million (English pounds or more than $4.5 billion).

("Any foreseeable expansion of the economy, even under a Tory Government, could not, in my view, be expected to produce the full amount which the Health Service requires in addition to what we are now spending." He said that the major portion of the cost of the National Health Service is borne by the taxpayer.)

Q. How much more money should Great Britain be spending on its National Health Service to make it a more effective service?

A. It is not possible to answer that question, because the health care of a people is an open-ended committment. The sources are always limited so that you'll never have enough. The decision as to how fast one develops and how much one devotes to health service is not a politician's decision, but a decision of the people.

(In his speech, Mr. Macmillan declared: ". . . as a country, we need to spend more on health—and that this extra money can only come from the people, whether we pay it as patients, as insurers, at rate-payers, or as taxpayers. In the end we pay; and we get the health service we are willing to pay for.")

Q. You don't think that the National Health Service is likely to break the Government financially, do you?

A. No. No! While it's a lot, it's not as much as aid to the regions.

Q. If the Conservative Party were to come out against National Health Service or try to abolish it, would it cause the defeat of the party at the polls?

A. It's like saying to a dragon: Will you eat people? The National Health Service is not something that . . . can be taken out or taken in. It's a system of controls that has grown up from the old days of the voluntary hospitals, as well as methods we had before, going back to Elizabethan days . . . There's no question of the health service being abolished. Can you abolish traffic? It's there.

Q. Then the National Health Service will remain regardless of which party is in power?

A. There has never been any question of this at all. We invented it. Winston Churchill set up Lord Beveridge's committee in the middle of war to look into the whole postwar development. The National Health Service was one of the products of that committee. So from the very beginning it was supported by every party. It was the fruit of the Coalition Government.

(The fourth report in the series discusses the position of the British Medical Association on the National Health Service.)

FROM THE EXECUTIVE DIRECTOR'S OFFICE

William R. Richards, M.D.
Executive Director

160 St. Ronan Street, New Haven, Conn. 06511
Telephone 865-0587

Josephine P. Lindquist
Associate Executive Director

CALL

ANNUAL MEETING OF THE HOUSE OF DELEGATES

The 1970 Annual Meeting of the House of Delegates will be held in the Terrace Room of the Hartford Hilton Hotel, Hartford. The first session of the House of Delegates will commence at 8:30 o'clock in the morning of Tuesday, May 12, with reference committee hearings at 11:45, followed by luncheon. A special program will be held at 2:30 P.M. and the House will reconvene at 4:00 P.M. for the completion of business.

Stevens J. Martin, President
Kenneth F. Brandon, Speaker of the House
Reginald C. Edson, Secretary

INTRODUCTION OF RESOLUTIONS

Article V, Section 12, Par. 3 of the Bylaws of the Society Provides that:

> *All resolutions to be considered as regular business at any regular meeting of the House of Delegates must be in the hands of the Speaker not later than seventy-two hours before the opening of that meeting. All resolutions and recommendations published in the official agenda distributed to the members of the House prior to the meeting at which action is to be taken shall be considered as regular business. Resolutions presented later than seventy-two hours before the opening of a meeting will be referred for consideration as regular business by the House only when they are presented by the Council or accepted for consideration by majority vote of the delegates present. Any resolution which does not qualify in accordance with the aforesaid provisions for consideration as regular business may be accepted for action by a majority vote of the delegates present and, if so accepted, shall be referred at once by the Speaker to a reference committee. Any such reference committee shall consider resolutions referred to it and shall report, with recommendations to the House before adjournment of the meeting.*

PROPOSED AMENDMENTS TO THE BYLAWS

The following proposed amendments to the Bylaws were presented to the House of Delegates on December 11, 1969 and were tabled for consideration and action at the next regular meeting of the House of Delegates.

In accordance with the Bylaws, these amendments will be published in Connecticut Medicine, "on one or more occasions prior to the next meeting . . . at which meeting the amendment shall be taken off the table and acted upon by the House of Delegates."

Introduced by the Council

I. COMMITTEE ON STATE LEGISLATION

Purpose: To reorganize the Committee on State Legislation to facilitate primary study of bills by experts in the various fields who are on the committee, rather than referring bills for study to other committees.

Amendment

ARTICLE XI—Divisional Boards and Committees

Section 5—Duties of Standing Committees

Par. 8. The Council annually shall nominate to the House of Delegates a Committee on State Legislation to consist of not less than sixteen members, including at least one member from each county, and shall nominate the chairman thereof. The members, insofar as feasible, shall be capable of representing the various speciality divisions of medicine. The functions of the committee shall be to study and review proposed state legislation. . . .

Present Bylaw

Par. 8. Committee on State Legislation. Annually before the fifteenth of January, each component association shall send to the Executive Director of The Society its nomination of an Active Member of The Society to membership on the Committee on State Legislation. The Council annually shall transmit these nominations to the House of Delegates and, in addition to these eight nominees, the Council shall nominate to membership on the Committee the Delegates to the American Medical Association and shall nominate the chairman of the committee. The function of the committee shall be study and review proposed state legislation. . . .

II. LIFE MEMBERSHIP

Purpose: To include in the Bylaws the action voted by the Council that Life Members may be exempt from the payment of dues on January 1 following their 65th birthday.

Amendment

ARTICLE IV—Membership

Section 4—Life Membership (Add the following sentence)

Exemption from payment of dues for Life Members shall become effective on January 1 of the year following the thirty-fifth year of membership or of the anniversary year of their sixty-fifth birthday, whichever is applicable.

III. ELECTION OF PRESIDENT-ELECT AND OTHER GENERAL OFFICERS

Purpose: To remove the necessity of election of officers by ballot and leaving the choice of method of election to the House of Delegates.

Amendment

ARTICLE VI—General Officers

Section 3—Term of President-Elect (Delete the underlined words)

The President-Elect shall be elected annually by ballot by the House of Delegates ....

Section 4—Terms of General Officers (Delete the underlined words)

Par. 1. Election. The Vice-President, the Secretary, Treasurer, and the Speaker and Vice-Speaker of the House of Delegates shall be elected annually by ballot by the House of Delegates . . ..

The House of Delegates shall elect by ballot Delegates and Alternate Delegates ....

IV. VACANCIES

Purpose: To provide for filling of a vacancy in the office of Vice-President.

Amendment

ARTICLE VI—General Officers

Section 4—Vacancies. (Add the underlined words)

Par. 2. In the event of a vacancy in the office of Vice-President, Secretary, Treasurer or Vice-Speaker or Delegate or Alternate Delegate to the American Medical Association, the Council shall fill the vacancy . .....

V. DUTIES OF THE PRESIDENT

Purpose: To delete the statement that the President preside at all meetings.

Amendment

ARTICLE VI—General Officers

Section 8—Duties of the President. (Delete the underlined words and add words in capitals)

The President shall preside at all meetings of the Society. He THE PRESIDENT shall be an ex-officio member of all committees. He shall appoint all committees not otherwise provided for in these Bylaws, subject to confirmation by the Council . ...

VI. POWERS AND DUTIES OF THE COUNCIL

Purpose: To provide for the Council to employ necessary legal counsel without directives from the House of Delegates.

Amendment

ARTICLE VII—The Council

Section 1—Powers and Duties

Par. 11. Counsel. (Delete underlined words and add words in capitals)

The Council shall employ legal counsel and or a legislative agent subject to the directives of the House of Delegates AS NECESSARY IN THE PERFORMANCE OF ITS DUTIES.

VII. DUTIES OF THE EXECUTIVE DIRECTOR

Purpose: To delete the words "Clinical Congress", which is no longer a mandatory annual meeting, and to clarify the duty of the Executive Director to keep records of CSMS committee meetings.

Amendment

ARTICLE VII—The Council

Section 3—Executive Director

Par. 2. Duties (Substitute the following paragraph)

Sub-Par. (g) To record attendance and proceedings of all meetings of the House of Delegates, the Council, and other official meetings of The Society and to maintain records of all meetings of committees of The Society.

Present Bylaw

Sub-Par. (g) To record attendance and proceedings and maintain records of all meetings of the House of Delegates, the Clinical Congress, the Council, and committees of the Society.

VIII. SCIENTIFIC ASSEMBLY

Purpose: To remove the provision that the Council arrange the scientific assembly. This function is now carried out by the Committee on Program of the Scientific Assembly.

Amendment

ARTICLE VIII—Scientific Assembly

Section 2—Meetings

Par. 1. General. (Delete the underlined words and add words in capitals)

General meetings of the Scientific Assembly OF THE SOCIETY shall be held annually. General meetings of the Scientific Assembly shall be arranged by the Council which shall select the persons to preside. AT A TIME AND PLACE DESIGNATED BY THE COUNCIL. THE ANNUAL MEETING OF THE HOUSE OF DELEGATES SHALL BE HELD DURING THE WEEK OF THE SCIENTIFIC ASSEMBLY.

IX. ORGANIZATION AND OPERATION OF BOARDS AND STANDING COMMITTEES

Purpose: To facilitate the preparation of the budget of the Society.

Amendment

ARTICLE XI—Divisional Boards and Committees

Section 4—Organization and Operation of Boards and Standing Committees (Delete the underlined words)

Each divisional standing committee shall submit to its divisional board for transmittal to the Council a budget for the fiscal year.

Per Directive of House of Delegates
December 11, 1969

X. CHANGE IN DIVISIONAL BOARDS

Purpose: To combine the present Legislation and Public Relations Divisions in a new Public Affairs Division under which the following committees would be included:

Committee on State Legislation
Committee on National Legislation
Committee on Public Relations
Committee on Public Affairs (New)

Amendment

ARTICLE XI—Divisional Boards and Committees

Section 1—Divisions (Delete the following divisions)

Legislation Division
Public Relations Division
(Add the following Division)
Public Affairs Division

Section 3—Divisional Standing Committees (Delete the following paragraphs in their entirety)

Paragraph (B) Legislation Division
Paragraph (E) Public Relations Division
(Add the following Paragraph)
Public Affairs Division
  Committee on State Legislation
  Committee on National Legislation
  Committee on Public Relations
  Committee on Public Affairs
(Reletter paragraphs as necessary)

Section 5—Duties of Standing Committees (Add the following new numbered paragraph)

Committee on Public Affairs. The Council shall annually nominate to the House of Delegates a Committee on Public Affairs to consist of not less than eight members and shall nominate the chairman thereof. The function of this committee shall be, in consultation and cooperation with the Committee on State Legislation, the Committee on National Legislation, and the Committee on Public Relations, to plan a program of political education for members of The Society, such program to be conducted on a year-round basis and to be implemented by the office of the Executive Director. The Committee shall also maintain liaison with the Board of Directors of the Connecticut Medical Political Action Committee (COMPAC) and shall encourage support of COMPAC among the members of The Society.

DELEGATES TO ANNUAL MEETING:

The Bylaws of the Society provide that each county association is entitled to one delegate in the House of Delegates for each thirty-five Active or Life Members in the association or fraction thereof based on the membership as of December 31st of the immediately preceding year. In order to be eligible for membership in the House of Delegates, a physician must have been an Active Member or Life Member of The Society for at least two years immediately preceding the session of the House in which he is to serve. According to this, the quota of delegates from each county association who should attend the Annual Meeting of the House of Delegates which will be held in Hartford, May 12, 1970, and the Semi-Annual Meeting in December, 1970 is as follows:

County	Membership Dec. 31, 1969	Official Delegates
Fairfield	1005	29
Hartford	1164	34
Litchfield	150	5
Middlesex	125	4
New Haven	1043	30
New London	218	7
Tolland	32	1
Windham	75	3

ELECTION OF COUNCILORS AND ASSOCIATE COUNCILORS:

Councilors and Associate Councilors, who shall serve for two years, shall be elected this year at the annual meeting of each of the county associations in Fairfield, Litchfield, New Haven and Tolland counties. In accordance with the Bylaws, each component association having over 750 members may elect one additional Associate Councilor. Therefore, the Fairfield and New Haven County Medical Association's should elect a Councilor and two Associate Councilors for a two year term.

No Councilor or Associate Councilor elected by a component association shall serve more than three successive terms of two years each in his respective office, but after a lapse of one term of two years, such Councilor or Associate Councilor shall be eligible for reelection.

Newly elected Councilors and Associate Councilors shall not assume office until after the Annual Meeting of the House of Delegates.

In the event that both the Councilor and the Associate Councilor(s) from a county association cannot be present, the President of the county association may appoint a substitute councilor.

SUMMARY OF ACTIONS
COUNCIL MEETINGS

Wednesday, January 21, 1970

I. Attendance

*Present were: Drs. Granoff, Weber, Jr., Edson, Brandon, Abbot, Dean, Fabro, Polivy, Rogol, Cramer, Gallo, Harwood, Petrie, Purnell, Roch, Grant, Nemoitin, Friedberg, Johnson, McDonald, Pelz, Root, Jr., von Glahn, Palomba and Klare.

Also present were: Mrs. Lindquist, Dr. Hess (Welfare Department), Mr. Donelan (AMA) and Dr. Richards.

Absent were: Drs. Martin, Gardner, Wilson, Jr., and Gorin.

*In the absence of Stevens J. Martin, Chairman and President, due to illness, the meeting was chaired initially by Morris A. Granoff, President-Elect, and later by Kenneth F. Brandon, Speaker of the House, who was elected to the newly-created office of Vice-Chairman of the Council.

II. Routine Business

Approval of Minutes

As printed and distributed, it was VOTED to approve the minutes of the meeting of November 19, 1969, with the correction that Robert L. McDonald, LCMA Councilor, is to be recorded as "present" instead of "absent".

Life Memberships

It was VOTED to approve applications for Life Membership received from the following eligible Active Members:

Alphonse A. Beatrice, Bristol (HCMA)—1970
Eugenia Cameron, New Haven (NHCMA)—1970
Max M. Gould, Southington (HCMA)—1970
George M. Gura, Hartford (HCMA)—1970
James C. Hart, Hartford (HCMA)—1970
Otto M. Hirschfield, Hartford (HCMA)—1970
Raymond T. Houle, East Hartford (HCMA)—1970
William Mendelsohn, New Haven (NHCMA)—1970
Charles S. Mirabile, Hartford (HCMA)—1970
Philip J. Moorad, New Britain (HCMA)—1970
Leslie E. Morrissett, Richmond, Virginia (FCMA)—1970
Milton J. E. Senn, New Haven (NHCMA)—1970
Joseph G. Uricchio, Hartford (HCMA)—1970
Ellwood C. Weise, Sr., Bridgeport (FCMA)—1970
Hyman W. Winters, Bristol (HCMA)—1970
John H. Winters, West Hartford (HCMA)—1970

Resignations, Appointments, etc.

(a) *Committee on Occupational Health*: It was VOTED to accept the resignation of Jack J. Albom, New Haven, as a member of this Committee.

(b) *Judicial Committee*: It was VOTED to appoint Kurt Pelz, Wallingford, as a NHCMA representative on the Committee, replacing Clyde L. Deming, New Haven, deceased, for the balance of the term 1968-70.

(c) *Ad Hoc Committee to Study Group Practice*: It was VOTED to appoint George J. Geanuracos, Bridgeport, to membership on this Ad Hoc Committee.

(d) *Committee on Allied Medical Services*: It was VOTED to accept, with regret, the resignation of Stewart J. Petrie, Derby, as a member of this Committee.

(e) *Vice Chairman of the Council*: By unanimous consent, Kenneth F. Brandon, Hartford, was elected to the office of Vice-Chairman of the Council (as required by an amendment to the Bylaws adopted by the House of Delegates on 12/11/69).

(f) *Committee on Public Affairs (pro tem)*: As authorized by the House of Delegates on 12/11/69, it was VOTED to elect a Committee on Public Affairs, *pro tem*, and that the Chairman, in consultation with other members of the Council, be authorized to name the members of the Committee and designate the Chairman thereof. The members shall be "not less than eight" in number. The Chairman appointed the following Committee:

Kenneth F. Brandon, 151 Farmington Avenue, Hartford, Chairman
E. Tremain Bradley, 31 Stevens Street, Norwalk
Bernard A. Burnham, 1389 West Main Street, Waterbury
Luca E. H. Celentano, 442 Elm St., New Haven
Eugene H. Corley, 1026 Park Ave., Bridgeport
Isadore H. Friedberg, 93 Market Sq., Newington
Francis Gallo, Medical Arts Building, Winsted
Max R. Goldstein, 111 Pearl St., Hartford
Timothy F. Nolan, 49 Lake Ave., Greenwich
George E. Roch, 132 Mansfield Ave., Willimantic
James H. Root, Jr., 1389 West Main Street, Waterbury

III. Old, New and Special Business

Election of Student Members

It was VOTED to elect to Student Membership twelve residents of Connecticut who are attending medical schools in the United States. A list of those elected will be published in the Journal.

Pursuant to this action, it was further VOTED to refer to the Subcommittee to Study and Revise the Bylaws, for comprehensive study and report to the Council, the entire subject of student membership, including eligibility requirements, limitations of rights and privileges, etc. In part, this action was taken in light of the current national trend (several state medical societies) to accept students, interns and residents as regular Active Members except for the obligation to pay membership dues.

Committee on Public Affairs, Pro Tem

As recorded previously, it was VOTED to direct the Chairman to appoint at least eight members of a newly-authorized Committee on Public Affairs and designate the chairman thereof. In related actions:

(a) It was VOTED to receive as information, and to approve in principle, a letter submitted by James H. Root, Jr., Waterbury, concerning the new Committee, COMPAC and matters pertinent thereto. It was further VOTED to reaffirm the Council's support of COMPAC and to advocate that the existing COMPAC agency be reorganized and revitalized; also, to direct the Committee on Public Affairs, in consultation with COMPAC representatives, to study and report to the Council on recommended plans for the future role to be played by COMPAC, both as an affiliate of AMPAC and in its relationships with the Society.

(b) It was VOTED to accept a progress report filed by the Ad Hoc Committee to Study CSMS State Legislative Program, and to transmit the report to the Committee on Public Affairs as information and for possible guidance.

Presentation of Award—Commissioner Bernard Shapiro

Due to former Welfare Commissioner Shapiro's inability to be present at the meeting a certificate for service (authorized by the Council and the House of Delegates) was accepted by Charles Polivy, Hartford, for personal delivery to the Commissioner. In making this presentation *in absentia*, Morris A. Granoff, President-Elect, read the certificate's inscription as follows:

> "The Connecticut State Medical Society extends greetings to Commissioner Bernard Shapiro and awards him this certificate in recognition of his continuing efforts, while State Welfare Commissioner, to improve the quality and conditions of medical assistance available to the underprivileged of Connecticut and to work in partnership with the medical profession toward this goal."

Implementation—House of Delegates Resolution re Hospital Cost Control

It was VOTED to charge the Committee on Public Relations with responsibility of drawing up and implementing a program of internal communication to the membership urging physician participation (with hospital administrations) in efforts to control the cost of hospital care services, and to furnish the membership with "guidelines" for such participation; also to request the Committee on Hospitals to furnish to the PR Committee recommendations concerning the drafting of suitable "guidelines" to be publicized for this purpose.

Pursuant to these actions, it was further VOTED to request the special Ad Hoc Committee on Hospital Costs and Related Matters to file a subject report with the Council forthwith (by February 19th if possible).

Resolution—Milford Medical Society

It was VOTED to receive as information, with interest and with thanks, a resolution adopted by the Milford Medical Society which commends Mr. George Plaskowitz, Administrator of the Milford Hospital, for the "creditable job" he has done in keeping hospital service costs down at that institution, and to notify Mr. Plaskowitz that the action of the Milford Medical Society has been brought to the attention of the Council and that the Council extends congratulations to him for having received this expression of confidence from the community physicians of Milford.

It was further VOTED to bring this action of the Council to the attention of the Committee on Hospitals with the recommendation that the Committee explore with Mr. Plaskowitz the methods he has used to control costs at the Milford Hospital (including assistance rendered by members of the medical staff) and file a subject report with the Council at its next meeting on February 19, 1970.

Report—8th International Congress of Gerontology

It was VOTED to accept as information, and with thanks and commendation, a report on the proceedings of this Congress (Washington, D.C., 8/24-29/69) filed by Alexander J. Tutles, chairman of the CSMS Committee on Aging, who attended as a representative of the Society. It was further VOTED to request Dr. Tutles, after discussing the report with the members of his Committee, to prepare an abbreviated version of it for publication in the Journal.

Accreditation of Hospitals

It was VOTED to refer to the Committee on Hospitals, for study and report, a question raised by J. Alfred Fabro, Torrington, concerning possible duplication and/or conflicts in the accreditation of hospitals that may be occurring as a result of independent inspections of hospitals being conducted by the State Department of Health and the Joint Commission on Accreditation of Hospitals.

Position re P.A. 713 (69)

Public Act 713 (69) provides a requirement that industrial health clinics and student health services be licensed by the State Health Department, and authorizes the Public Health Council to develop and promulgate regulations concerning such licensure. The P.H. Council has published proposed regulations in the Connecticut Law Journal, and the Committee on Industrial Health has expressed criticism of, and suggested changes in, those regulations. On recommendation of the Committee, the Council VOTED to adopt the following resolution:

WHEREAS: The legislature of the State of Connecticut has enacted legislation to require the licensing of Industrial Health facilities; and

WHEREAS: The Public Health Council has advertised certain regulations in order to implement this legislation; and

WHEREAS: The enactment of these regulations will affect the functioning of all private occupational health facilities providing services to thousands of the state's industrial workers; therefore be it

RESOLVED: That the Council of the Connecticut State Medical Society urge the Public Health Council to withhold approval of the proposed regulations until such time as:

1. A public hearing can be held by the Public Health Council, or
2. Consultation can be held between the Commissioner of Health, officials of the Connecticut State Medical Society, its concerned committees and leading occupational physicians regarding these regulations.

State Legislation

(a) It was VOTED to request the Committee on State Legislation to give careful review to all measures (held over from the 1969 General Assembly as well as new ones which might or should come before the 1971 session) in which the Society may have a major interest in 1971, including those for which it would be advisable for the Society to sponsor bills rather than support or oppose those introduced by others and to report on same to the Council.

(b) It was VOTED to request the Ad Hoc Committee to Study Abortion and Sterilization to prepare a "position paper" on the subject of sterilization and offer recommendations concerning the appropriate provisions of a bill to be sponsored by the Society in 1971 which will be in keeping with the position advocated and accomplish its purposes.

(c) It was VOTED to request the Committee on State Legislation (via the staff) to solicit from the County Medical Associations, from the committees and sections of the Society and from the general membership suggestions for specific legislative actions (subjects, bills, etc.) which are felt desirable for the Society to take at the 1971 session of the General Assembly.

(d) It was VOTED to direct the Committee on State Legislation (via the staff) to solicit "position papers" on subjects of legislative concern from appropriate committees of the Society for the purpose of establishing or updating the Society's legislative policies toward such subjects.

(e) It was VOTED to request the Advisory Committee on School Health, through the parent Committee on Public Health, to furnish the Committee on State Legislation (and the Council) with an up-to-date position paper on health education (including family life and "sex" education) in the schools.

(f) It was VOTED to authorize Isadore H. Friedberg, chairman of the Committee on State Legislation, to pursue with Rep. Lavery, co-chairman of the Assembly's Health Care Study Committee, Mr. Lavery's invitation to have informed members of the Society meet with his Study Committee to discuss health and medical care matters of mutual interest.

Nominee to P.A. 754 (69) Examining Board

P.A. 754 (69) creates a new examining board for the licensing of nursing home administrators, one of whom shall be selected from among nominees of the Connecticut State Medical Society. At the request of Commissioner Franklin M. Foote, State Health Department, the Council VOTED to nominate (for appointment of one member) the following three physicians.

George E. Roch, Willimantic
Alexander J. Tutles, Hartford
Frederick C. Weber, Jr., Greenwich

Committee on Hospitals

It was VOTED to approve and comply with a request submitted by the Committee on Hospitals that it receive any and all materials discussed and/or acted on by the Council which pertain to hospitals or professional practice within hospitals.

Proposed New Medicaid Regulation

A communication received by the President, Dr. Martin, from the Ohio State Medical Association bringing to the Society's attention their opposition to a newly proposed regulation for Medicaid, which would become effective April 1, 1970, requiring a physician to sign a disclaimer on all Medicaid claims, stating the following: "This is to certify that the foregoing information is true, accurate, and complete. I understand that payment and satisfaction of this claim will be from Federal and State funds, and that any false claims, statements or documents, or concealment of a material fact, may be prosecuted under applicable Federal or State laws", was discussed. It was VOTED to receive this communication as information, since the deadline for filing opposition to the regulation had already passed. The AMA also opposed this regulation on the basis that, "physicians will consider the new requirements an unwarranted affront to their integrity".

Air Pollution

A communication received by the President, Dr. Martin, from the Chairman of the Medical Society of New Jersey Committee on Environmental Health, pointing out that New Jersey "shares common air sheds with Connecticut, New York, Pennsylvania and Delaware" and urging these states to address themselves to their air pollution control commissions or administrations, strongly recommending that the air quality levels be brought into conformity with New Jersey's more stringent code was presented. It was VOTED to refer this matter to the Committee on Public Health for study and report, and ultimately, to the Committee on State Legislation for appropriate action prior to, and during, the 1971 session of the General Assembly.

Guests—Council Meeting

On recommendation of Charles Polivy, Councilor-at-Large, it was VOTED to extend an invitation to Mr. Joseph L. Gordon, Executive Director, Hartford County Medical Association, Mr. Arnold Olson, Executive Secretary of the Fairfield County Medical Association, and William L. West, M.D., Clerk of the New Haven County Medical Association, to join the Council as guests at all meetings.

N.B.: *The foregoing is a summary of the proceedings and actions of the Council on January 21, 1970. Detailed minutes of the meeting are on file at 160 St. Ronan St., New Haven, for perusal by any interested member of the Society.*

Placement Opportunities

PHYSICIAN who will be willing to work on a salary basis for one or two years with an opportunity for subsequent full partnership after approximately three additional years. Practice consists of general-medical pediatric type practice with the exclusion of obstetrics and major surgery.

CHEST CLINIC PHYSICIAN—35-hour week. $18,520-$22,846. Excellent fringe benefits. Training available as needed. Contact R. C. Edson, M.D., State Health Department, 79 Elm Street, Hartford, Connecticut 06115.

MEDICAL DIRECTOR—business equipment manufacturing concern. Well-equipped and staffed medical departments. Comprehensive occupational health program. Liberal fringe benefits. Salary negotiable. Contact Medical Director, Royal Typewriter Company, Division of Litton Industries, Hartford, Connecticut 06106.

GENERALIST OR INTERNIST—Growing central Connecticut residential community, fine schools, quiet country living. Twelve miles from 400 bed general hospital. For further information write or call William B. Lyons, M.D., R.D. #2, Kettletown Road, Southbury, Conn. 06488, Tele. 264-8884.

CONNECTICUT-PSYCHIATRIC RESIDENCIES—Community oriented, geographically unitized, mental hospital. Emphasis on Clinical Psychiatry. Training in Individual, Family and Group Psychotherapy. Expert supervision from senior faculty; affiliation with Yale University Medical School. AMA approved program, in a joint commission-approved hospital. Outstanding visiting lecturers. Automated records system and closed circuit T.V. Stipends: First year, $9323; Second year $9817; Third year, $10,694. Liberal benefits; housing available for a modest charge. Write to Mehadin K. Arafeh, M.D., Superintendent, Connecticut Valley Hospital, Box 351, Middletown, Connecticut.

VACANCIES FOR PART-TIME PHYSICIANS—Tours of duty are available to provide coverage on our Intermediate (Extended Care) Service evening, nights and weekends. Examples: 5:00 p.m.-8:00 a.m. (Weekdays)-$81.00 per tour; 8:00 a.m.-8:00a.m. (24 hrs. Sat or Sun. or Holidays)-$129.60 per tour. Interested physicians may make arrangements for intermittent or varying part-time tours of duty provided acceptable coverage is maintained during these periods. Part-time tours salary will be prorated according to above rates. Physicians must be U.S. citizens or possess permanent visas, and have licensure in one of the States. Write, visit or telephone: Chief of Staff, Intermediate Service or Personnel Officer Veterans Administration Hospital, West Spring Street, West Haven, Connecticut 06516—933-2561.

VACANCIES FOR FULL-TIME PHYSICIANS—Position open for Physician on Intermediate Service to provide supervision for rehabilitation and extended care for chronically ill patients. Physician must be U.S. Citizen or possess permanent visa, and have licensure in one of the States. Write, visit or telephone: Chief of Staff or Chief, Intermediate Service or Personnel Officer, Veterans Administration Hospital, West Spring Street, West Haven, Connecticut 06516—933-2561.

PEDIATRICS—Board certified or eligible wanted for association with Board man in a Connecticut shoreline community of 50,000. Close proximity to Yale Medical Center. Salaried first year, then partnership.

CAMP PHYSICIAN—for approximately 300 summer campers (boys and girls) at Winchester Center, Connecticut. 8 weeks period, beginning late June, 1970; would accept two physicians for consecutive four-week periods. Two R.N.'s in resident attendance. Salary open. Requirements: Must have Connecticut License; may be intern, resident, in practice or retired; with or without family.

MEDICAL DIRECTOR—40 hour week! All holidays! Regular vacations! No nights! All staff and equipment paid for by company. In short a high level professional staff position for a General Practitioner or Internist with a leading industrial firm in North Central Connecticut. Industrial experience not required but even part time exposure would be a plus. Will deal with various industrial health and safety problems and supervise a staff of five. Solid, well run firm. Excellent benefit program. Fine opportunity to grow. Starting salary $25,000. Naturally, all fees are paid by the client company. For completely confidential interview send curriculum vitae or call UNI/SEARCH, 15 Lewis Street, Hartford, Connecticut; 278-8040.

STUDENT HEALTH—Two immediate openings, University of Connecticut; competitive salary; campus of 14,000 in ideal rural setting; excellent fringe benefits and retirement; new wing being completed; access to all New England sports. Apply: Edward P. Wanderse, M.D., Acting Director, Health Service, University of Connecticut, Storrs, Connecticut 06268.

HILLSIDE HOME AND PRACTICE—Yalesville, Ct., midway between New Haven and Hartford. Location of 13 room, 3 story original farmhouse cannot be duplicated. Adequate space for office in home with 2-car garage, private garden area and panoramic view 15 miles to the East. Physician needed in the growing community between Wallingford and Meriden. Price $50,000 includes office equipment. For further information contact William W. Dickinson, M.D., 63 Hill Avenue, Yalesville, Connecticut 06492.

Placement Wanted

PATHOLOGIST—34 years of age, with National Boards wishes to practice in solo, group or associate type practice in Connecticut. Military obligations completed. Particularly interested in sea shore location. Presently in practice.

SURGERY—35 years of age, eligible with National Boards wishes to practice in solo or associate type practice in Connecticut. Military obligations completed. Presently in practice. Particularly interested in sea shore location. Available immediately.

NEUROLOGY—29 years of age, eligible with National Boards wishes to practice in solo, group or associate type practice in Connecticut.

INTERNIST—38 years of age, Board eligible wishes to practice part time or full time position with hospital as Hematologist in Connecticut. Military obligations completed. Available immediately.

SURGERY—35 years of age, Board eligible wishes to practice in group or associate type practice in Connecticut. Presently in practice. Military obligations completed. Available immediately.

INTERNAL MEDICINE—GASTROENTEROLOGY—33 years of age wishes group or associate type practice in Connecticut. Will consider partnership in the Fairfield area. Eligible with National Boards. Military obligation completed.

SURGERY—32 years of age wishes solo or associate type practice in Connecticut. Military obligation completed. Eligible with National Boards. Presently in practice.

OBS & GYN—33 years of age wishes solo, group or associate type practice in Connecticut. With Connecticut license.

ANESTHESIOLOGY—34 years of age wishes solo type practice in Connecticut. Certified with National Boards. Presently in practice. Interested in directing a department of Anestheseology. Available immediately.

EMERGENCY ROOM—39 years of age wishes to practice in Connecticut. Passed National Boards. Military obligation completed in July 1970. Connecticut license.

SURGERY—36 years of age wishes group or associate type practice in Connecticut. Military obligation completed. Certified with National Boards. Presently in practice.

UROLOGY—37 years of age wishes institutional type practice in Connecticut. Interested in a full time academic post. Eligible. Presently in practice. Available immediately.

GENERAL PRACTITIONER — 32 years of age wishes emergency room position in Connecticut. Presently in practice. Military obligations completed. Connecticut license in process.

PATHOLOGIST—39 years of age with Connecticut license seeking directorship of laboratory of similar position. Has eight years experience as laboratory director. Available when right position arises.

UROLOGIST—31 years of age with National Boards wishes group or associate type practice in Connecticut. Military obligation completed.

PHYSICIAN—43 years of age interested in emergency room or as a house physician in the Fairfield area. Eligible with National Boards. Available immediately.

INTERNIST—30 years of age with National Boards wishes associate type practice in Connecticut. Military obligation completed.

OB & GYN—30 years of age. Eligible with National Boards wishes group or associate type practice in Connecticut. Available in July when military obligation completed.

INTERNIST—35 years of age wishes group or associate type practice in Connecticut. Eligible with National Boards. Presently in practice as chief of medicine. Available in July when military obligation completed.

UROLOGIST—31 years of age wishes group or associte type practice in Connecticut. Eligible. Military obligation completed.

DERMATOLOGIST—30 years of age wishes solo, group or associate type practice in the Fairfield County area. Certified with National Boards. Presently in practice. Available when military obligation completed in July.

GENERAL SURGERY—33 years of age wishes group or associate type practice in Connecticut. Certified with National Boards. Available when military obligation completed in July.

INTERNIST—31 years of age wishes to practice in Connecticut. Available upon request.

RADIOLOGIST—34 years of age wishes group or associate type practice in Connecticut. Eligible with National Boards. Military obligation completed.

OPHTHALMOLOGIST—31 years of age wishes group or associate type practice in Connecticut. Eligible with National Boards. Presently in practice. Available when military obligation completed in July.

DERMATOLOGIST—35 years of age wishes group type practice in Connecticut. Presently in practice. Certified. Available in July.

ORTHOPEDICS—31 years of age wishes group or associate type practice in Connecticut. Eligible. Available in July.

RADIOLOGIST—31 years of age wishes group or associate type practice in Connecticut. Eligible with National Boards. Available when military obligation completed in June.

INTERNIST—31 years of age wishes group or associate type practice in Connecticut. Eligible with National Boards. While serving in the Air Force he held positions as Chief of Medicine and Chief of Hospitals. Presently in practice. Available when military obligation completed in July.

MEDICAL DIRECTOR—54 years of age wishes institutional type practice in Connecticut. Eligible. Presently in practice. Connecticut license.

ANYONE INTERESTED IN THE ABOVE IS ASKED TO CONTACT THE PHYSICIANS PLACEMENT SERVICE, 160 ST. RONAN STREET, NEW HAVEN, CONNECTICUT 06511.

The Connecticut State Medical Society offers placement assistance through the Physicians Placement Service, 160 St. Ronan Street, New Haven, Connecticut, 06511. This service is for the use of physicians seeking locations, as well as physicians seeking associates, and is without charge.

AROUND THE STATE

New Haven County

Board of Governors Meeting
New Haven County Medical Association

January 29, 1970

The New Haven County Medical Association Board of Governors met at The Colonial House in Hamden on Thursday, January 29, 1970 under the Chairmanship of President Kurt Pelz.

Our Councilor, Stewart J. Petrie, brought the board up to date on the Connecticut State Medical Society's Council meeting of January 21, 1970. Dr. Petrie announced that Kurt Pelz had been appointed to fill the unexpired term of the late Clyde L. Deming on the Connecticut State Medical Society Judicial Committee. The proceedings of the Council are presented in detail elsewhere in *Connecticut Medicine*.

Considerable discussion at the meeting centered about the increasing costs of hospital care, the need for revitilization of COMPAC, and new plans for the format of the business part of the annual county meeting to be held on March 19, 1970 at the Waverly Inn.

The combined executive and ad hoc committee to contract for the services of a professional public relation's firm is continuing its investigations and will begin interviewing firms in February.

The final format of the by-laws changes to be proposed by the Board of Governors at the annual meeting were voted after the usual lengthy debate that by-laws changes inevitably evoke.

The procedures to be followed in implementing New Haven County's Compulsory Attendance program were spelled out and approved by the Board.

Efforts to improve relations between the Association and the auxiliary have been started.

Bernard Burnham, Chairman of the New Haven County Medical Association Committee on State Legislation made a detailed presentation of the political and legislative scene in the Congress and emphasized the improvement over the years of the relationship between organized medicine in Connecticut and their Congressmen from Connecticut.

Following the social hour and dinner, another group of provisory members were indoctrinated into active membership. New Haven County's current membership now stands at 1,043.

Respectfully submitted,
William L. West, M.D., Clerk

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2. Weekly benefits up to $250.00 cannot be reduced by company once issued.
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First Vice-President
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Mrs. Joseph C. Czarsty, Oakville

Recording Secretary
Mrs. Gabriel Ingenito
Corresponding Secretary
Mrs. Stanley J. Weigel, Danielson
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Mrs. Edwin R. Connors, Pawcatuck

To provide medication at the lowest possible cost to victims of kidney disease, the Kidney Foundation of Connecticut maintains a Drug Bank program. Its services are open to all patients who are residents of the state, through their physicians.

All medication offered and available through the Drug Bank is first approved by the Foundation's Medical Advisory Board, whose president is John A. Goffinet, M.D. The list of drugs is up-dated periodically, and may be obtained upon request.

In every category the Foundation has a trade name product and, when available, a generic drug produced by Wolins Pharmacal Corporation, whose drugs are accepted by F.D.A. and presently are used in more than 1,000 hospitals in the United States.

The Kidney Foundations furnishes physicians with registration forms to be filled in for each patient. Information also is provided on the exact cost of each prescription, so that the patient knows the charge before ordering.

The physician returns the completed registration blank; the patient sends prescriptions and payment to the Foundation office. A new Rx must accompany each drug order.

Medication is mailed out to the patient directly from the pharmacy. The arrangement safeguards the normal relationship between the physician, the patient, and the pharmacist.

The Kidney Foundation neither prescribes nor recommends medication. Drugs are supplied at actual cost to the agency, which assumes mailing and handling charges. The Drug Bank currently is serving patients in all parts of the state.

A non-profit health agency, the Foundation maintains headquarters in New Haven at 357 Whitney Avenue. Richard L. Ranaudo is Executive Director.

Units of the chapter are active in the Hartford, Waterbury, Bridgeport, Norwalk, Stamford, Meriden and New Haven areas, where volunteers will campaign for funds during March. The agency has a state-wide goal of $100,000. The annual Trick or Treat candy promotion, more successful each year, will be held in October.

An affiliate of the National Kidney Foundation, the Connecticut chapter also supports research into the causes, incidence, treatment and cure of all kidney diseases. Through grants from the national organization, one young scientist is being supported for his second year at the Yale University School of Medicine, and another man will begin study there in July.

The Foundation also makes grants to hospitals for the purchase of special equipment needed in the care and treatment of renal patients, and conducts public and professional education programs.

don't miss the

178th ANNUAL C S M S MEETING

May 12, 13, 14, 1970

Hartford Hilton Hotel, Hartford

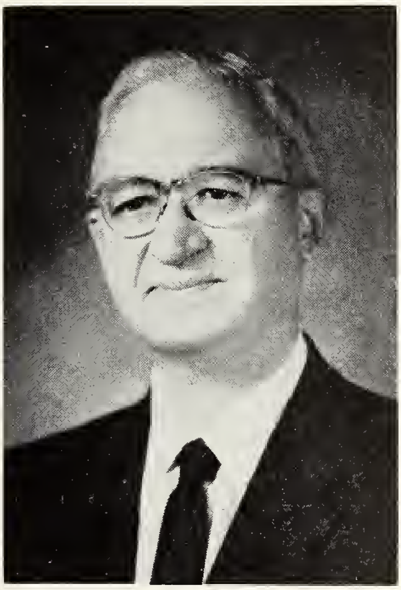
—: PLAN NOW TO ATTEND :—

OBITUARIES

J. Whitfield Larrabee, M.D.
1895-1969

"Whit" Larrabee attained a goal which he set for himself early in life: a career in medicine.

Dr. Larrabee was born in a rural area of Prince Edward Island, Canada. He came to the Boston area of the United States to finish his secondary schooling and "go to Harvard". He was graduated from Harvard College, and then from Harvard Medical School in 1926. During most of this period he was completely self-supporting, and while in Medical School he worked as an attendant at Massachusetts' McLean Hospital. He then came to Hartford, Connecticut, for his internship of 22 months at Hartford Hospital. At the end of this period, he made two decisions which strongly affected his later life. First, he decided to remain in the Hartford area. He settled in the Elmwood section of West Hartford with his first wife, a Hartford Hospital graduate nurse, and began the general practice of medicine. Dr. Larrabee was well-liked in that rapidly-growing community, and quickly became very successful. He also maintained an office in downtown Hartford.



During this period, he became friendly with the late Dr. James C. Wilson, who practiced orthopedics in Hartford. Dr. Wilson invited him to assist with the orthopedic service at the Hartford Municipal Hospital (now McCook) and this association led to his second important decision—namely, to become a trained and certified orthopedic surgeon. During World War II, with a diminished staff at Hartford Hospital, he was given an appointment in the Department of Orthopedics, and also the Newington Home for Crippled Children (now Newington Children's Hospital). With this experience in specialized surgery, he realized that additional training was necessary so, with the cooperation of his family, he gave up his general practice in order to study the specialty at New York's Hospital for Special Surgery. After examination, he was certified by the American Board of Orthopedic Surgery, and two years later became a Fellow of the American Academy of Orthopedic Surgery. He had attained his goals.

In 1947, Dr. Larrabee entered into a ten year period of pleasant and productive orthopedic practice (with the author) until a severe coronary attack forced his retirement. During this period he participated vigorously in the orthopedic programs of both Hartford Hospital and Newington Children's Hospital. His circle of personal friends was large, and he found pleasure in serving on the Medical Directors' Staff of Sphinx Temple, A.A.O.N.M.S. Dr. Larrabee was a member of the Hartford Medical Society and the Connecticut State Medical Society.

Early during his orthopedic practice, tragedy struck his family when his wife was killed in a plane crash. He later married Mrs. Phyllis Holt, who survives him and with whom he has had a very happy life for nearly twenty years. He is also survived by three children: John W. Larrabee, Jr., of Bedford, New Hampshire; Nathaniel Larrabee II, of Holliston, Massachusetts; and Mrs. Victor Carpenter, of Philadelphia, Pennsylvania; and eight grandchildren.

His passing on December 28, 1969, was sudden and quiet at his home.

Maurice M. Pike, M.D.

Michael J. Conroy, M.D.
1896-1969

It is with greatest sorrow that we announce the death of Dr. Michael J. Conroy.

"Mike", as he was affectionately known to his friends, had a distinguished career. He was graduated from the Meriden High School, received his bachelor's degree from Yale University in 1918 and his medical degree in 1920. After a year's surgical internship at Long Island Hospital of Medicine in Brooklyn, N.Y. he became associated with the department of Pathology at Yale Medical School. Later he served as instructor in pathology at Harvard Medical School. Following this he was a resident surgeon at the Good Shepherd Hospital in Syracuse, N.Y.

Dr. Conroy then returned to Meriden where he confined his work to surgery. He was Chief of Surgery for three years at Meriden Hospital; subsequently, he was Chief of Staff. He was certified by the American Board of Surgery and became a Fellow of the American College of Surgeons.

He had been president of the Meriden Medical Society and the New Haven County Medical Society; a member of the Connecticut State Medical Society and the A.M.A.

The city was saddened when it learned of his death. His hundreds of patients and friends will find it difficult to replace him in their hearts.

We, his colleagues shall miss "Mike's" warm personality, his kindness, charity and compassion for his fellow man. Indeed we have lost a dear friend and associate.

Those who knew Dr. Conroy admired his brilliant mind, his love of music, his excellence in golf and his devotion to his family and patients.

He was proud of his family, his two sons, members of the medical profession, Dr. John Thomas Conroy, anesthesiologist at Hartford Hospital and Dr. Michael M. Conroy, a surgeon in Meriden; his daughter, Marietta, a Doctor of Philosophy, on the faculty of the College of Saint Teresa, Winona, Minnesota. Another daughter, Mrs. Robert Mills, predeceased her father. His lovely wife, Marietta Cashen Conroy, was a source of inspiration and solace to him.

The following are excerpts from the editorial which appeared in the *Meriden Morning Record* at the time of Dr. Conroy's death.

"Dr. Conroy practiced more than medicine; he practiced the Golden Rule, solidly, concretely, constantly and modestly. He was concerned with his patients as fellow human beings, not just with their ailments. He listened to them, not just to their hearts. He listened to what was in their hearts. They poured out their problems and their anxieties into his patient, discreet ear, and they went away feeling better for having had a sympathetic listener."

We quote from Browning, who said, "All conscience and all courage."

Raymond V. Quinlan, M.D.

In Memoriam

Frank, Harry S., Middletown, College of Physicians and Surgeons, Columbia University 1924. Dr. Frank was a surgeon in the Middletown area for many years. Dr. Frank was on the staff of the Middlesex Memorial Hospital and Rocky Hill Veterans Hospital. He served in World War I. Dr. Frank was a member of the American Medical Association, the Middlesex County Medical Association and the Connecticut State Medical Society. Dr. Frank died January 17 at the age of 69.

Roccapriore, Benjamin A., Middletown, Jefferson 1931. Dr. Roccapiore was a general practitioner in the Middletown area for 36 years. For the past 28 years, he was the public school physician and a member of the Middletown Board of Health. He was an attending physician of the Middlesex Memorial Hospital Staff. During World War II, he served with the U.S. Navy, taking part in the invasion of Okinawa. Dr. Roccapriore was president of the Central Medical Association, a member of the Middlesex County Medical Association, American Medical Association, Connecticut State Medical Society and the American Academy of General Practice. Dr. Roccapriore died January 3 at the age of 64.

Zaglio, Edmond R., Manchester, College of Physicians and Surgeons, Columbia University 1933. Dr. Zaglio was an orthopedic surgeon in the Manchester area for more than three decades. Dr. Zaglio was appointed attending orthopedic surgeon at Newington Children's Hospital in 1931. He joined the courtesy staff of Manchester Memorial Hospital and the Rocky Hill Veterans Hospital in 1936. He was named assistant in orthopedic pediatrics on the active staff of Manchester Memorial Hospital in 1938; he became an associate in pediatrics in 1946, and he was named chief of orthopedics in 1949.

Dr. Zaglio served 27 months during World War II as a captain in the Army Medical Corps at a base hospital in the Aleutian Islands. Dr. Zaglio was a member of the American Medical Association, the Hartford County Medical Association and the Connecticut State Medical Society. Dr. Zaglio died January 9 at the age of 61.

News From Yale University School Of Medicine

Dr. Fredrik C. Redlich, Dean of the Yale University School of Medicine, has issued the following statement commenting on what he thinks are the good and bad features of the recently introduced drug bill (S. 3246) in the U.S. Senate, proposed by Senator Thomas Dodd (Conn.) and the Nixon Administration:

I am delighted that Senator Thomas Dodd is making a significant effort to attack the problem of drug abuse and reformulate the legal framework surrounding drug problems. All of our efforts to date have not done enough to help rehabilitate drug addicts and stem the influence of drug peddlers. But we must look closely at all the implications of this bill, being sure that it is aimed at the basic problems of drug abuse, and that it embodies the best thinking in medicine and psychiatry.

A good feature of the bill is the establishment of an expert committee to study marijuana. There is significant new research available which might call for a reappraisal of our predominantly legal approach to marijuana.

Another good feature is the elimination of mandatory minimum jail sentences for drug users. We should know more, however, about the complimentary feature of the bill—the promise of stiffer penalties for drug peddlers. We must be sure that the law differentiates between the narcotic addict who only occasionally sells drugs and the major peddler or distributor. The possibility of suspended sentences, probation and parole for drug users is not new with this bill. In sum, the penalties for different kinds of drug abuse and abuse of different kinds of drugs must be restructured, but we must be sure that such penalties allow room for justice and rehabilitation as well as punishment of the most dangerous drug peddlers.

There are several features of the bill that deserve even closer scrutiny, and which, at first blush, do not seem desirable additions to our drug control laws.

The transfer of power from health oriented agencies such as the Department of Health, Education and Welfare, and the Food and Drug Administration, to enforcement oriented agencies such as the Justice Department does not seem entirely desirable. This proposal comes just when many persons in the drug field are coming to realize that drug abuse is a health problem—a problem of sickness and rehabilitation—as much as, or even more than it is a legal problem. This may be a step backward, just as more physicians are becoming active in drug treatment programs.

The addition of Librium, Valium and meprobamate to the list of controlled drugs is necessitated by what the Senator has called the significant misuse and substantial diversion of such drugs into illegal channels. If it can be conclusively demonstrated that there is significant abuse of these drugs, and substantial diversion into illegal channels, then they should be so regulated. If not, however, we may be merely adding one more round of paperwork to the practicing physicians' desk.

Finally, I would like to hear good evidence that the "no-knock" provision of the law will result in significantly more arrests of pushers being made than are now made. Unless this can be shown, I would have some doubts about this particular aspect of the bill.

Medical costs will continue to climb but more people will be getting less medical care unless the financing is drastically reorganized.

That's the warning of three faculty members of the Yale School of Medicine.

"Some form of organizing the financing of medicine is an absolute necessity because medical care is beyond the economic reach of even the working families," according to Dr. Richard Weinerman, Professor of Public Health and Medicine.

"Health services are consuming something like $57 billion annually in this country," but "there will be a greater degree of inequality in medical care because of rapidly rising costs unless there is an increased government role in providing health care," states Rosemary Stevens, Assistant Professor of Public Health.

"The problem isn't that we are spending too much," according to Dr. Richard Granger of the Yale Child Study Center, but rather that we "are distributing it improperly."

Another problem, according to Dr. Granger, is that "most of our care is being concentrated in the cities, and within the cities it is not being distributed equally to the poverty areas."

He said that "the number of doctors available in rural communities has gone down in the last 30 years by almost half."

Dr. Weinerman warned that "national health insurance by itself could freeze" the present maldistribution of resources and inequalities in the health system. He said that he doubted that "any kind of health insurance system is going to solve the problems all by itself."

Prof. Stevens agreed that "an insurance scheme as a collecting agency would freeze existing patterns," and that it "would not necessarily help the poorer areas of the country and rural areas."

She said that the solution was a combination of a national health insurance agency with "a system of incentives and controls," such as "incentives for hospitals and other facilities, group practice, health centers and other different ways of providing health care."

Dr. Granger noted that his recent experience of 15 years in the practice of pediatrics lead him to appreciate the financial inefficiency of private practice. He said that the "high overhead for the practitioner is passed onto the patient." He also said that "this is one of the reasons that medical costs are rising so high." His solution to this problem would be to "group doctors and facilities where they can share overhead more reasonably."

Dr. Granger noted that his own bias was in favor of "improving ambulatory care facilities, because they are the least expensive kind of facility to build, to staff, and the kind of care that can be given there can prevent the necessity for the more expensive care that is occasioned by neglect.

"A lot of the younger physicians who are being trained are changing their viewpoints. New medical students have a responsible attitude toward the social welfare of patients, more so than many of us have had in the past," he said.

The three agreed that an essential part of any planning to restructure medical care was a strong degree of local control. They also felt that "any system set up should give the medical patient consumer a large voice in how it is done."

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MEETINGS

GENERAL

May 12, 13, 14
178th Annual Meeting
Connecticut State Medical Society
Hartford-Hilton Hotel, Hartford

MEDICINE

Weekley Oncology Courses **12 Noon**
Hospital of St. Raphael, Radiation Therapy Conference Room

March 19
Carcinoma of Female Breast
Radiation Therapy; Wayne P. Whitcomb, M.D., Chemotherapy, David S. Fischer, M.D.

March 26
Case Presentation

April 2 **5:00 P.M.**
Connecticut Cytology Society and the Connecticut **Division, American Cancer Society**
Park Plaza Hotel
The Cytologic Criteria of Malignancy
Guest speaker John K. Frost, M.D., Director of Cytopathology, John Hopkins Hospital
Peter Bent Brigham Postgraduate Medical Series

April 10 **8:30 A.M.-5:30 P.M.**
Congestive Heart Failure
Pathophysiology and Therapy, Richard Gorlin, M.D,. Chief, Cardiovascular Division

May 8 **8:30 A.M.-5:30 P.M.**
Clinical Application of Lung Function Tests
Harry Bass, M.D., Director, Pulmonary Division

SURGERY

May 6, 7, 8
43rd Annual New York Eye and Ear Infirmary Clinical Conference
Biltmore Hotel, New York City
Held in conjunction with the 150th anniversary celebration of the New York Eye and Ear Infirmary. An open house will be held at the New York Eye and Ear Infirmary on Saturday, May 9, featuring scientific exhibits and demonstrations of newer instrumentation and techniques.
Contact Jane Stark, Executive Secretary, 310 East 14th Street, New York, New York 10003

NEW BOOKS IN REVIEW

HUTCHISON'S CLINICAL METHODS, 15th EDITION.

Edited by Donald Hunter and R. R. Bomford. J. B. Lippincott Co., Philadelphia, 1969. 404 pp. $7.00

Reviewed by: LOUIS H. NAHUM

This book is now on its 70th year and should continue to be of assistance both to medical students and post-graduates. It has undergone a complete and thorough revision. There is a new section on hearing and tests of auditory and vestibular function. There is a virtually new chapter on the examination of the eye and one on the examination of children. It is a conventional book detailing how to examine, what to look for, and what laboratory tests one requires to make a diagnosis.

Its philosophy is descriptive. When a student begins to work in a medical ward, he asks himself how shall I investigate this case. This book is intended to provide an answer. There is case taking in general and general schemes for the investigation of medical cases. There is an expansion of this theme, each system being taken up separately and the method of investigation described in detail. The book was originally written by Sir Robert Hutchison at the age of 25 in 1897, long before modern learning theory had been clarified.

The traditional approach to the teaching of principles and methods of clinical examination was quite deficient in that it stressed memorization. Modern notions of learning theory, however, suggest that factual information isolated from its context will be forgotten at a predictable rate. Learning is a process in which the individual must actively participate, a process which requires experience appropriate to the individual's needs as he views them, a process which moves at a pace dictated by the learner. Learning requires comprehensive retention and recall. It is facilitated by subsequent experience which reinforces the original learning process. It is fostered by motivations and extrinsic rewards.

The clinician must develop a hypothesis to explain the patient's symptoms and signs. Symptoms and signs are of value only in so far as they assist the physician to construct a hypothesis. Rewards should be given for the construction of conceptual models by deductive reasoning. In modern medicine function has achieved a peer position with structure in all discussions of health and disease. In this sense a philosophic approach to the clinical examination is needed for the conceptualization of disease, for the approach to the understanding of normal and abnormal biology and for effective learning principles.

Texts on clinical examinations that are currently being publishel reveal words and phrases reduced to adjuncts, eponyms are few, pictures representing classical disease states are omitted. Philosophic or dynamic concepts of health and disease receive the focus of attention. Clinical methods and the factual information of the preclinical sciences are made to contribute logically to the understanding of the concepts. Clinical diagnosis has been repositioned in the prominent position it deserves. The measure of the practioners proficiency in his skill in the clinical examination pertains to knowledge, ability and techniques necessary for accurate clinical assessment. Hutchison's text even though it is structural and not functional is to be considered an assist to the physician who is trained in dynamic concepts of disease processes.

THE ROLE OF LEARNING IN PSYCHOTHERAPY

(also an issue of the International Psychiatry Clinics). A Ciba Foundation Symposium. Edited by Ruth Porter. Little, Brown and Company, Boston 1969. 340 pp. with 30 illustrations. $12.00.

Reviewed by: LOUIS H. NAHUM

The Ciba Foundation was founded in 1949 to promote international cooperation in medical and clinical research. Every year the foundation organizes six to ten three day conferences and three to four study groups all of which are published in book form. This one is an especially felicitous symposium because there has been a paucity of objective and particularly controlled studies assessing the results of psychotherapy and also a lack of information about the factors that affect these results.

Two important factors that influence the outcome of psychotherapy is the unlearning of maladaptive habits and the learning of new and more appropriate behavior. In this book we find results of a meeting in which psychotherapists of different schools discussed their underlying theories, techniques and results. The views expressed were varied and at times emotional and hotly disputed. But the discussions were constructive, the participants were open-minded with a capacity for accepting each others points of view.

The extent of agreement between the protagonists of the different schools was at times surprising. The members of the symposium, all world authorities, examined together their various techniques in a liberal way. They also looked with scientific objectivity and with humanity for new ways of assessing their results, something hitherto almost impossible in psychoanalysis.

In general the participants represented two great traditions, that of Freud a great scientist and also a great clinician with remarkable insights; the other another scientific giant Pavlov who worked first in the laboratory but also in later years became interested in the clinical applications of his discoveries. Thus the participants were truly exposed to new ideas and new observations.

Some of the differences that have arisen in connection with psychotherapy may be because each school is examining a different part of the problem. Others may be due to the fact that we are dealing with dissimilar patients in different ways and have thus been observing and grouping together somewhat different phenomena. Other difficulties may be connected with the way terminology is employed. But the important thing recognized by all the participants was their aim to present material of which they were quite sure. In this respect the Pavlovians came out better than the Freudians.

Pavlov and Freud both had a great deal of courage and proceeded to develop their ideas against often bitter opposition. For example Neil Miller, the editor of this symposium recalled the time when Freud, then a very young man, tried to present to the Vienna Medical Society a case of hysteria in a male patient. He was jeered and hooted out of the room after an "old grey beard" said "Obviously the young doctor doesn't know his Greek: "hysteria" means "womb-sickness." It was a good story with which to introduce the participants who in a spirit of unorthodox courage and tolerance, tempered with critical realism analyzed the role of learning in psychotherapy both from the psychoanalytic and behavioral points of view.

THE PHYSIOLOGY OF OBSTETRIC ANESTHESIA. Gertie F. Marx, M.D. and Louis R. Orkin, M.D. Charles C. Thomas, Springfield, Illinois. 1969. 186 pp. with 12 illustrations. $12.00.

Reviewed by: FREDERICK W. HEHRE

The *Physiology of Obstetric Anesthesia* by Gertie F. Marx, M.D. and Louis O. Orkin, M.D. is an unusual little volume that is bursting with information that is succinctly presented. The text is well written, comfortably readable and is, above all, short. (6 chapters; 186 pages) The material has been organized into two logical categories: 1) Physiological considerations, and 2) Anesthetic considerations. Each major section has been subdivided and developed in relation to: 1) the mother; 2) the uterus and placenta; and 3) the infant. Within the latter divisions, subheadings have been extensively employed to focus the readers attention on specific problems.

The writer, Dr. Gertie F. Marx, is a recognized authority in the sub-specialty of obstetrical anesthesiology. Her literary style is clear, concise and brief, and, her complete command of the subject, as well as the pertinent literature, is obvious from the bibliographical annotations in every part of the text. She cites almost every article of real and/or recent significance in the field at least once. The extensive bibliography at the end of each chapter is of major importance particularly when one realizes the speed at which significant developments in fetal physiology are being reported.

It is a rare occurrence nowadays to find a clear presentation with pin-pointed and referenced information in such a small package. Unquestionably, this monograph is the currently definitive text in the field of obstetrical anestheisology. It is an absolute must for the library of every anesthesiologist and is strongly recommended for every obstetrician.

Recent Developments in Cardiac Pacing

In addition to the classical indication for cardiac pacing—heart block with Adams-Stokes attacks—atrial or ventricular pacing is now used for the control of other paroxysmal or sustained cardiac arrhythmias when drug therapy or direct current cardioversion is ineffective or is contraindicated. When properly used, pacers can prolong life and permit normal activity in most of the patients who would otherwise die or be disabled. Since The Medical Letter last reviewed cardiac pacing (Vol. 7, p. 78, 1965), new equipment with broader usefulness has been developed.

Fixed-rate pulse generators (American Optical; Cordis; Electrodyne; General Electric; Medtronic) are usually set at 60 to 70 beats per minute. Pacemakers of the "demand" or "standby" variety (American Optical; General Electric; Medtronic) have the same base rates, but halt stimulus discharge when spontaneous rates become more rapid. Pacers can also be activated by the absence of a spontaneous electrical impulse at a preset interval. Atrial synchronous pacemakers use an additional electrode to sense atrial depolarization and permit stimulation of the ventricle, thus producing an approximation of normal sinus rhythm.

Demand ventricular pacemakers are proving useful in some patients with intermittent heart block. Temporary cardiac pacing is also used, often in intensive care units, to prevent ventricular fibrillation and control atrial or ventricular tachycardias and, with demand pacemakers, to control bradycardias induced by such drugs as quinidine or digitalis.

TEMPORARY PACING—Temporary transvenous electrodes (Cordis; Electro-Catheter; Medtronic; United States Catheter & Instrument) for use with external pulse generators are inserted into a peripheral vein (subclavian, femoral, external jugular, or brachial) and either guided under fluoroscopy or floated with electrocardiographic monitoring into contact with the wall of the right ventricle or the wall of the right atrium. Some clinicians believe that the ease of application of the floating technique utilizing the Cordis or Electro-Catheter Semi-Floating electrodes, makes it the method of choice for emergency use (A. S. Rosenberg et al., Amer. Heart J., 77:697, 1969). Placement is more certain with fluoroscopic positioning, however. Temporary pacing is discontinued when the patient regains a stable rhythm.

Many intensive care units are now equipped with monitoring systems which include circuits for either fixed-rate or demand endocardial pacing for temporary control of arrhythmias, especially tachyarrhythmias. Alternatively, portable battery powered demand-type pulse generators (American Optical; Cordis; General Electric; Medtronic) can be used. After cardiac surgery, temporary pacing by removable myocardial wires can help to control arrhythmias and improve cardiac output.

Reprinted from *The Medical Letter on Drugs and Therapeutics*, New York, N.Y.

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Index to Advertisers

Arch Laboratories, St. Louis, Mo. — — — — — — — — 163

Bio-Chemical Procedures — — — — — — — — — — — 195

Burroughs-Wellcome, Tuckahoe, N.Y. — — bet 200 & 201

Campbell Soup Company, Camden, N.J. — — bet 184 & 185

Classified Advertising — — — — — — — — — — — — 219

Dentocain Co., Bloomfield, Conn. — — — — — — — — 219

Arthur W. Eade, Hamden, Conn. — — — — — — — — 211

Geriatric Pharmaceutical Corp., Floral Park, N.Y. — 9, 164

Hynson, Westcott & Dunning, Inc., Baltimore, Md. — — 3

Lederle Laboratories, Pearl River, N.Y. — 5, bet 200 & 201

Eli Lilly & Co., Indianapolis, Ind. — — — — — — FC, 10

McNeil Laboratories, Inc., Fort Washington, Pa. — — 147

Merck, Sharp & Dohme, West Point, Pa. — — 156, 157, 158

Mutual Land Management & Development, Inc.,
Westport Conn. — — — — — — — — — — — — — — IBC

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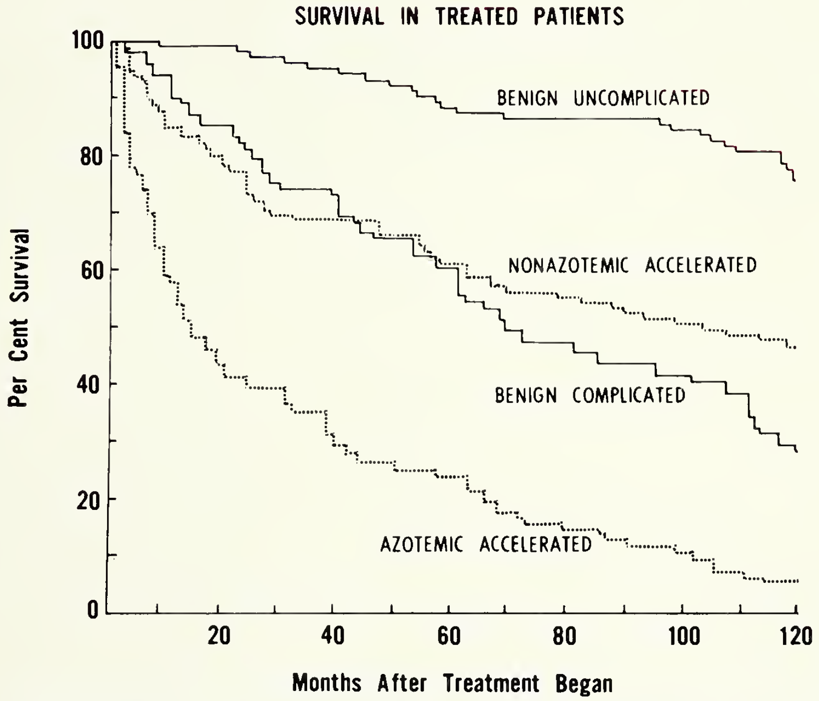
Volume 34/April 1970/Number 4



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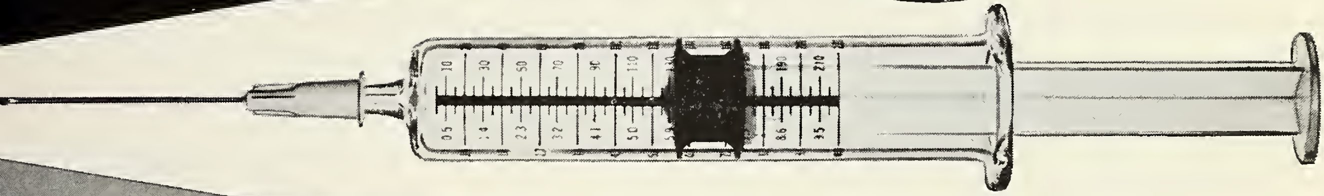

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CONTENTS

editorials

The Role Of The University In Medicine 221
Decisions In Hospital Law 224
Survival In Treated Hypertensives 226
Acoustic Trauma From Rock And Roll 228
The Tympanic Thermometer And Thermal Regulation . . 230
The Moon Dust 232
A Look Into The Future Of The Clinical Laboratory . . . 235
The Papilliary-Muscle Dysfunction Syndrome 236
Side Effects Of Detergents 237
A Look Into The Future Of Patient Monitoring 238

scientific

Problems In Cadavaric Donations For Renal Transplantation, *Martin Schiff, Jr., M.D., Bernard Lytton, M.D., Robert S. Brown, M.D.* and *John A. Goffinet, M.D.* 253
Rheumatoid Carditis, *Siegfried J. Kra. M.D.* and *Philip Fazzone, M.D.* 257
Acute Organic Psychosis Due To Talwin (Pentazocine), *Murray A. Yost, Jr., M.D.* and *F. Patrick McKegney, M.D.* 259
JeJunal Hematoma, Child Abuse, And Felson's Sign, *Marcel Bratu, M.D., John C. Dower, M.D., Bernard Siegel, M.D.* and *Salah H. Hosney, M.D.* 261

departments

The President's Page 250
From The Executive Director's Office 265
Physician's Placement Service 272
Woman's Auxiliary 293

miscellaneous

Program—178th Annual Meeting 241
Artists Attention 252
Around The State 276
Medical Grand Rounds—Yale-New Haven Hospital, Chronic Renal Failure Treated By Transplantation, *Frederick Lee Sachs, M.D.* and *Lewis Landsberg, M.D.* 277
Special Article
The Medical Profession And The Press, *Paul Gough* . . 287
X-Ray Of The Month, *Arnold B. Rilance, M.D.* 282
Electrocardiogram Of The Month, *Ira L. Rubin* and *Julian Frieden, M.D.* 284
British National Health Services, *New Thomas* 291

Connecticut Medicine

editorials

The Role Of The University In Medicine

The University is the target in the savage cross fire between uncritical lovers and unloving critics.—John W. Gardner[1]

Prior to 1910 medical schools considered their role to be educational—to train physicians to engage in private practice. In 1910 Flexner's report revolutionized medical education by instituting full time teachers and researchers in all clinical departments. Thus to teaching was added the role of advancement of biomedical science by the teachers. We are now in a new revolution. The question is posed whether our universities should continue their time honored role of teaching and research and also branch out into community service. The struggle to come then is science or service for it is obvious to everyone that too much service will undermine the time honored role of medical institutions in Science and training of experts.

There are inadequacies in our present system of health care. Medicare and Medicaid are in part responses to these. There is a difference in infant mortality and life expectancy in the disadvantaged areas. Continuing care for ordinary but pressing day to day problems increasingly strain hospital emergency rooms. The situation is aggravated by dislocations because of urbanization, an increasingly mobile population, rapid obsolescence of physical plants of hospitals. There is a rapidly expanding fund of biological knowledge and the impact of increasing technology is profound in what now can be offered to people in regards to health preservation. What challenges and what rewards will modern technology bring to the practice of medicine?

Medicine in the future must also help to cope with public health problems of enormous proportions that have been created by an increasing population through births and increased life expectancy, dwindling food supply in many areas, industrial hazards and pollution of our environment.

As medicine becomes more of a science this is bound to pervade and alter the actual practice of medicine. In a sense every encounter between physician and patient is an experiment. In both diagnosis and treatment physicians engage in very complicated problem solving in which many of the intellectual processes are still not clear enough for programming or computer. Can the scientific method then be applied more effectively to physician encounters so as to improve the outcome in terms of benefits to the patient? Can the depth of our culture also be brought to bear on these encounters so that the human condition of the patient as well as his physical condition be bettered?

Educational institutions are equipped to conduct scholarly inquiry and planning required to meet the challenges and by changing the goals and content of training programs to alter the organization of medical practice and delivery of medical care in a sound orderly manner. To meet the needs of the future, medical schools must

THE COVER

The figure gives the survival curves for 316 patients with varyingly severe hypertension treated with ganglioplegic agents and hydralazine. Solid lines indicate patients with benign stages of hypertension and dotted lines patients with accelerated stages of hypertension. The "crossover" of the curves for the benign complicated and non-azotemic accelerated groups after 3 to 5 years of therapy is intriguing since the accelerated group eventually has the lower mortality. The percentages to the right of the curves give survival figures for untreated but otherwise roughly comparable patients.

train a broad range of scientific physicians from medical administration on the one hand to psychiatrists on the other, from physicians who will practice in rural communities and health care centers, to medical school professors and research institute scientists. The schools in short must continue to advance medical knowledge and prepare a rigorous education for the wide range of future physicians.

Owing to the high costs, lack of qualified faculty and students and other obligations of medical schools, it seems unlikely that the number of graduating physicians will be increased dramatically in the foreseeable future. Such expansion as will occur will barely keep pace with minimal societal needs. Accordingly a wide variety of paramedical personnel will be required to undertake many aspects of medical care. Ideally the medical schools should undertake the training of these paramedical personnel. It will ensure a high level of technical competence, a team approach which involves the physician. It will institutionalize professional values in such personnal as a group. Professional values of high standards, ethical principles, self-discipline and service are important if social responsibility of the medical care system is to be maintained.

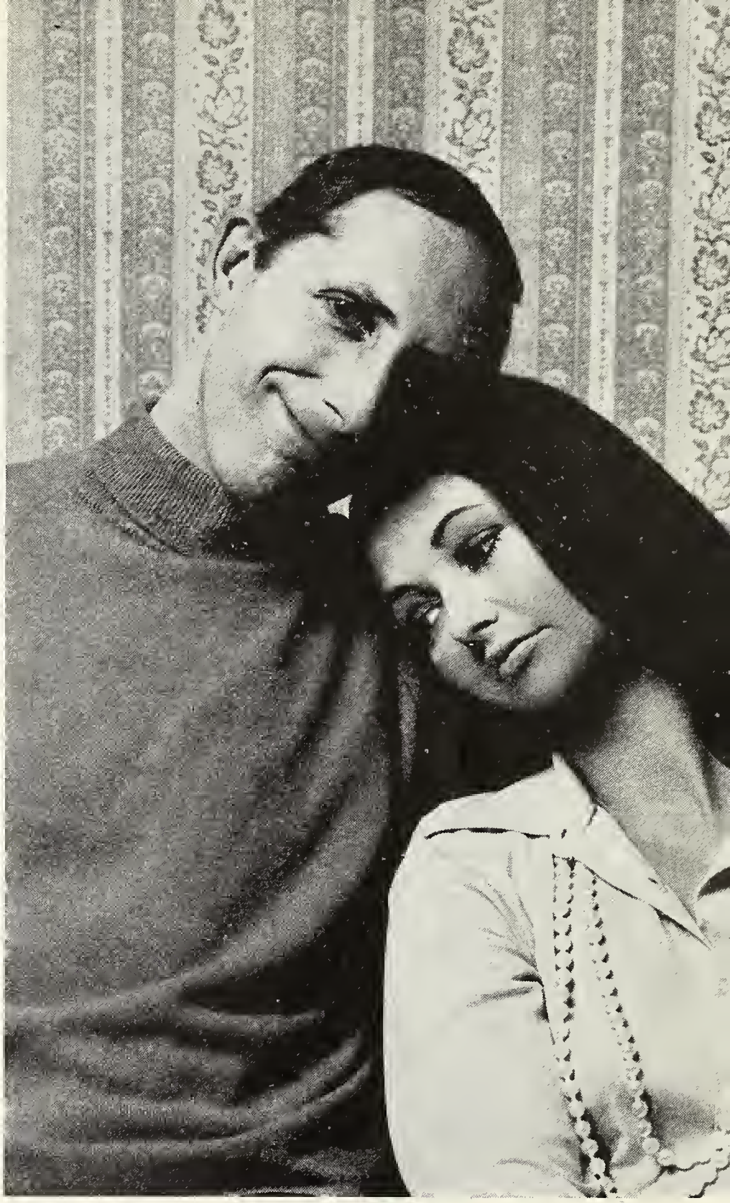
Because of their resources medical schools have come under enormous pressure to become increasingly engaged in the delivery of medical care. Knowledgeable educators are pondering to what extent medical schools can fulfill their responsibility to the community by delivering medical services without at the same time jeopardizing their responsibilities to the community in the area of scholarly research, long range planning and training of medical and paramedical personnel. Haggerty believes there are serious dangers to the university if it takes on too much of the care of an entire community. If, however, the university develops models for provision of primary medical care then other institutions in the community might be better able to carry such a program to its final application. For the university has even more compelling responsibilities than providing service. It has the responsibility to study carefully what it is doing and especially to develop the basic science of health care and to do whatever it does in such a way that its final responsibility, education, is not jeopardized.

After a decade of personal efforts to take the university out of its detachment and into the community Haggerty has concluded that the greater danger in the years immediately ahead are most likely to come from too much engagement and result in too little science in the area of health care especially programs for primary health care, than from too little service. The basis for the danger is obvious for without more science in the health field, it will never advance beyond its present status and with too large service demands upon the limited faculty there will be too little service.

There are two areas of science in primary medical care — health services research and epidemiology. If the university is to set up and deliver primary health care then it must evaluate the outcome of such programs. This is health services research. Haggerty points to many areas that need study such as needs, expectations, demands, utilization, outcomes of the services rendered. Why do people use health services when they do. Is there a variation on perception of illness by the individual and why. What is the outcome factor of treatment in terms of function of the individual. At Rochester they developed a 12,000 person care unit to study such questions. In this model unit they will strive to build theoretical models to explain health care systems. Such theoretical model building and testing is a luxury permitted in a university and one absolutely necessary if we are to come up with new thoughts into the reasons why people do and do not use health services.

No university should be engaged in primary care programs unless they are to be used for educational purposes and research. They will encounter problems, lack of continuity of care, community resistance and the difficulty in learning good clinical practice there. Neighborhoods want "real" doctors not students or residents. This will make it difficult to acquire clinical skills of diagnosing and managing the social and behavioral problems of patients. Such skills can be taught in primary care centers, but unless they are used for education, they have little justification in a university. It is probably not the universities role merely to provide such care.

It is obvious that if primary health care institutes are to be set up a special innovation in medical curriculum will have to be formulated. Unlike their docile predecessors, contemporary medical students tend to be activists, concerned with justice and social relevance. They will demand that the medical curriculum move rapidly



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in the direction satisfying the expectations of society. A community health care institute for studying community health problems should meet their expectations, and focus in their minds what a university should and should not do.

L.H.N.

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Decisions In Hospital Law

The Law courts have in the past accepted the proposition that "Hospitals do not practice medicine." The courts have asserted that only physicians can be licensed to practice medicine and therefore that hospitals can neither practice medicine nor can they control the actions of physicians. This proposition applied as well to dentists, nurses and other health professions who are legally licensed. However, Professor Curran points out that the law is changing.[1] A number of courts have now rejected the implication of the inability on the part of hospitals to practice or administer health services.

In one of the most important decisions in hospital law in many years the Colorado Supreme Court held a community hospital liable for the negligence of a registered professional nurse in administering an injection to a post-operative patient.[2] The court refused to hold the surgeon liable for the nurse's negligence on the mere fact that he had ordered the medication. He was, in fact, not even present in the hospital when the nurse administered the injection which struck the sciatic nerve and caused a permanent foot drop in the seven year old plaintiff. The court held the hospital liable because it was the employer of the nurse and had actually assigned the nurse to the particular service and had supervised the nurse in her duties.

Professor Curran points out that the principle of law under which the hospital was held liable is commonly known as "respondent superior" that is let the employer answer over the negligence of a servant or agent. The hospital argument was that the nurse's actions were professional in nature and therefore not answerable by the hospital. Justice Groves concluded "If we were to rule that 'respondent superior' does not apply because the hospital is not licensed as a nurse then it would seem to follow that an airline should not be liable for the negligence of its pilots because the airline is not licensed to fly an aircraft . . . . ." The hospital in this case was the employer of the nurse who committed the act. Only it had the right to hire and fire her. Only it could assign the nurse to certain hours, certain areas and certain patients. There was no choice in the doctor (defendent) or the plaintiff as to identity of the nurse who could serve (the child plaintiff). In this day and age a hospital should be responsible for the acts of its nurses within the scope of their employment irrespective of whether they are acting administratively or professionally.

There were several other aspects to the Bernardi decision. The court asserted that the plaintiff is entitled to receive by court-ordered discovery a copy of the hospital's "incident report" regarding the injury to the patient. The hospital could not prevent the plaintiff from obtaining a copy because of the fact that it might be useful to the defendent hospital's attorney in preparing their case in court. It was held that the primary purpose of the incident report is to report the facts of untoward injuries and losses to the hospital administration. As such they are hospital records and are subject to discovery and examination by the suing party.

Another important part of the Bernardi case was the rejection of a release of liability signed by the plaintiff's parents upon the admission of the patient. The Colorado Supreme Court ignored this language in a preoperative consent form signed by the parents and gave it no effect whatever in relieving the hospital of liability. A hospital is completely within its rights in requiring that a patient or his parents consent to an operative procedure after being properly informed of the nature and purpose of the procedure. However, the hospital cannot couple with this a complete release of liability on the part of the hospital for any negligence or other legal

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wrong doing. The court held that the patient or family clearly does not realize the meaning of the term "release" and therefore has no reasonable basis for granting it under the circumstances. The court therefore refused to enforce any such blanket release of liability.

Another problem raised about hospital liability concerns some aspects of physician coverage of the emergency room. Must a physician see an emergency room patient in person or can the nurse on duty see the patient, consult with the physician by telephone and advise the patient to return for a follow-up visit. It is true that a number of emergency room visits do not really require the immediate presence of a physician. Nevertheless, if the hospital is going to furnish first-class medicine the physician on duty should actually see the patient except in the most clear cut type of situation. Should complications develop subsequently and the patient was not seen by a physician the courts could impose liability upon the hospital.

In a case involving Montefiore Hospital in New York[3] a patient arrived with symptoms of a heart attack. Since the patient was a member of the HIP the hospital informed him that he was not eligible for hospitalization and offered to get in touch with a HIP doctor for him. The HIP doctor talked to the man by telephone and told him to go home. He died of a heart attack shortly thereafter and both the hospital and the physician were found liable.

Another case involving a Wilmington Hospital in Delaware is that of a family of a child with a high fever and who tried to get hold of the family doctor but were unable to reach him. They brought the child to the emergency room where the nurse on duty said that the child should be admitted by his own physician. The child died before the physician could be located and again the hospital was held liable.

Mr. Tilson[3] points out that there is no statute in Connecticut on emergency room coverage. However, the Public Health Code simply Provides that each general hospital must be so organized as "to provide adequate care for persons with acute emergencies at all hours." However, in view of the cases mentioned above it is probable that if the emergency room physician fails to see the patient and unfortunate circumstances thereafter arise the physician and the hospital may both find themselves liable.

L.H.N.

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Survival In Treated Hypertensives

Dr. Perry has collected data on 316 hypertensive patients whom his group observed for periods of 7-13 years. The patients all suffered from diastolic hypertension and varied from benign uncomplicated to accelerated or malignant hypertension that had progressed to azotemia. The survival rate depended upon the degree of recent impairment and the success in controlling the diastolic pressure. If the blood pressure was controlled, that is the diastolic pressure brought down to below 100, this mortality over 7-13 years was 50 per cent. If the blood pressure was only partially controlled—diastolic 100-110, mortality rose to 80 percent for 7-13 years. If the diastolic was not controlled and remained over 120, the mortality was 100 per cent over this period of observation.

It is clear then that the effective control of hypertension seems to be associated with the lessening of the severity of the underlying hypertensive process. However, since severity of hypertension is not easy to quantitate, it is difficult to provide convincing evidence for such a change. Perry reports a case age 34 with diastolic of 170 brought down to 90 by apresoline and hexamethonium who remained well only to die of myocardial infarction four years later. On the other hand he reports a lessening of severity in a group of 114 patients who continued the antihypertensive drugs. If their response was good and their diastolic was brought down to below 100, it was possible to gradually reduce the antihypertensive medication until after three years they required half of the original amounts of the drug in 70 per cent of these patients.

Another question is whether there are individuals with prolonged and essentially complete remission of hypertension. In Perry's series 16 out of the 316 patients did eventually develop a normal arterial pressure without help of medication. Initially they required 450 mg of apresoline and 2 grams of hexamethonium. The remissions were of gradual onset. Some of these 16 were of the accelerated type at the beginning of therapy. These patients were relatively young, mostly under 48 when the anti-hypertensive treatment was begun.

An all too frequent story is that of a patient with accelerated hypertension and azotemia and normal-sized kidneys. A few years back he had moderately high diastolic pressure but little else. Therapy was started but the patient felt well and did not consider himself seriously ill and failed to appreciate the importance of continuing his therapy. Gradually, however, his pressure rose, renal function declined until he had irreversible loss of renal mass. If he had recognized the future hazard, and importance of anti-hypertensive therapy, treatment would have staved off renal failure and prolonged his life.

Unfortunately such patients almost always progress to eventual renal failure. In a distressing number of instances the progression seems to occur suddenly and without warning. A consistently high diastolic pressure in such a patient therefore warrants enthusiastic therapy with all its attendant inconveniences and risks. Therapy should be begun with an explanation that marked lowering of blood pressure is usually associated with certain unpleasant side effects. Initially, at least, the patient will probably be unhappy. It requires a very good salesman to take a patient who feels well, make him feel temporarily bad and at the same time convince him that he is really better.

To be effective in such a situation, the physician must be convinced in his own mind that his patient's blood pressure demands effective control. Some patients with the accelerated type of hypertension develop a temporary rise in the BUN and decrease in creatinine clearance after their diastolic is decreased below 100. It is true that BUN may rise the first two weeks, but it generally returns to pretreatment levels the next two weeks. Greater increases, however, are ominous. One cannot relax the therapy, but as a temporary measure, it may be necessary to resort to dialysis.

Desipte the plethora of anti-hypertensive agents, none is really ideal, but the measure of their worth is the success in lowering the diastolic pressure. Today, most physicians begin with guanethidine, but it induces wide postural swings in pressure. For the patient who must

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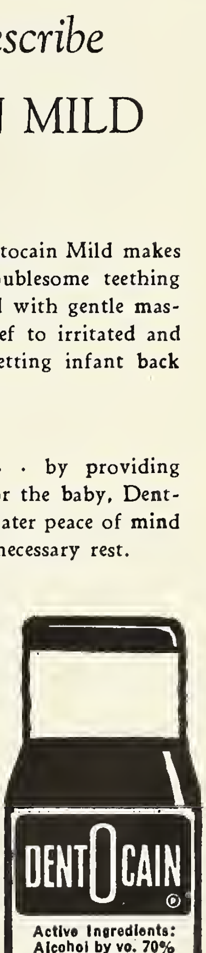

protect every remaining nephron, this obviously is less than ideal. Perry has come to place great reliance on hydralazine. Alone it does not provide adequate control and something more, a ganglionic blocking agent, usually must be added. Seven of the 16 remissions were in patients who developed arthralgia as a manifestation of delayed toxic reaction due to hydralazine. It appears that those patients who develop toxic reactions to hydralazine are more prone to remit.

It is interesting in considering the hypertensive causes of death that renal failure or cerebral hemorrhage was responsible for 75 percent of the uncontrolled group, for half among the partially controlled group, but for less than one-quarter among the controlled group. In contrast atherosclerotic causes of death appeared not to be influenced by the efficacy of anti-hypertensive therapy, accounting for no more than 10-15 per cent in each group. Both the causes of the deaths and their temporal distribution make it tempting to speculate that anti-hypertensive therapy alleviates hypertension and lessens death related directly to hypertension, but such therapy appears to do relatively little for atherosclerosis which continues to progress unabated. In treating patients with diastolic hypertension, it will not be sufficient merely to control the hypertension, but we must also deal with the removable causes of atherosclerosis as well, and the so-called risk factors must also be dealt with effectively.

L.H.N.

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Acoustic Trauma From Rock And Roll

Researchers have over a decade provided basic research and public education on the problems of industrial noise, but the medical profession has only recently begun to call attention to the probability that certain music groups using powerful electronic amplification have done and are doing irreparable damage not only to their own ears but also to the ears of their listeners.

There are two major concerns with acoustic trauma. One is that it is insidious, and the other is that individuals vary widely in susceptibility. In practical terms, this means that the threshold of pain is no good indication of whether one's ears are being permanently insulted. Furthermore, any damage-risk criterion for an "average" ear does not necessarily apply at all to a particular ear.

Another aspect of the insidious nature of the insult is that our spoken conversations have a built in safety factor of about 25 decibels (db). National committees, as well as the everyday observations in our office practice, agree that unless an ear's loss exceeds 25 db on the average, over 500 to 3000 cycles per second (c/s), that ear can hear ordinary conversation in a quiet room fairly well, with neither the talker nor the listener aware of any abnormality. However, an ear with a loss of 25 db is on the borderline of social competence. For speech that is garbled, interrupted, speeded, partially masked, such an ear is far from normal because it requires more or less frequent "repeats" to keep conversation flowing.

Thus, an ear originally perfectly normal could suffer a permanent loss of as much as 25 db for speech before it would be identified as beyond normal limits by the usual standard speech audiometric examinations in the otoaudiological clinic. Such a loss may well develop insidiously over a period of months. Enough cases have now come to our attention of such incipient handicapping losses possibly arising from the acoustic trauma of rock music, to make it advisable to look into what was known of an objective nature on this matter.

Rupp and Koch[1] recorded overall sound-pressure levels of 110 to 120 db in one rock-band rehearsal room, and found that all the musicians had "ringing" or a "sensation of fullness" lasting for eight hours to several days. To establish this fact experimentally in order to show a noxious effect, they need to know the dominant frequency which, to have a really noxious effect requires them to be in the general region of the maximum sensitivity of the ear.

Dey[2] decided to create acoustic conditions of rock music in the laboratory and study its effect on the hearing of young adults with the use of acceptable standards of experimental rigor and generality. He examined the question whether acoustic trauma is being produced by typical rock music and if so, what percentage of young ears would be expected to be injured by various sound intensities and durations. He measured many levels, the relative strength of each octave.

He administered music to fifteen men age 18-25 to one ear in combinations of both sound pres-

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sure level and session duration. Then they recorded auditory fatigue and the recovery curve. He found that fatigue increases in a linear fashion as sound levels increase. He used recordings of music played by a typical rock and roll band in a discotheque for young adults. The sound pressure levels in the octaves most damaging to hearing were of the order of 105 db.

Tape loops of this sound were then presented to the young men with normal hearing levels at 100-110 db for 5-120 minutes. With the use of temporary threshold shifts of 40 db after 2 minutes of recovery as a damage risk criterion, the data clearly indicates that after listening for 2 hours to such music at 100 db, 2 persons in a 100 would recover far too slowly whereas at 110 db, 16 percent would be adversely affected and probably permanently.

Dey takes a conservative figure for damage risk criterion of 40 db that must not be exceeded. Ward, et al[3] already showed that exposure to 50 db resulted in breakdown or at least a long drawn out phase of the recovery process as compared with recovery from 40 db. On this basis it can be seen that the damage-risk criterion is considerably exceeded by the average man exposed for 2 hours to the 120 db level.

There are individual differences. But Dey's criterion should protect 84 per cent of the population exposed for two hours at 110 db, a condition not uncommon in discotheques generally. But this will leave an unusually severe hearing damage in about 16 per cent of young men exposed. To protect all the young people adequately the sound level would have to be about 100 db. What even this exposure would do to an already damaged hearing can be safely predicted to be harmful, although this was not tested by the authors.

It is not likely that health authorities would insist that our young people restrict themselves to so mild a sound as 110 db for two hours. We shall have to reconcile ourselves to damaging the 16 per cent most susceptible. People tend to live as though their personal pleasures will not lead to invalidism later. We know, however, from bitter experience with smokers, guzzlers, gluttons, that the pay off is inevitable in the form of invalidism and that a time comes when they become burdens on family and society and require social rehabilitation and social support.

L.H.N.

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The Tympanic Thermometer And Thermal Regulation

In 1958 two new methods for research on thermoregulation were first applied in concert. One was human calorimetry by means of the gradient principle and the other was the measurement of the central temperature in man at the tympanic membrane. Calorimetry permitted rapid recordings of total flow rate of human heat loss with differentiation between heat loss by evaporation of sweat and heat loss by radiation and conduction-convection.

After much critical thinking, Benzinger's[1, 2] site of choice for the measurement of central temperature was the tympanic membrane of the ear. It is located midway between the surface of the head and sagittal midplane, close to the stem of the internal carotid artery which supplies the brain and the thermoregulatory centers in the hypothalamus. The tympanic membrane is accessible by suitable probes without discomfort, is always dry, and lends itself to thermoelectric measurements with clean, disposable sensors. The sensor is a simple disposable junction of copper and constantan of the loop type for direct contact with the ear drum.

Clinical experience with disposable tympanic sensors is now rapidly growing. First, it was necessary to compare tympanic membrane temperatures with rectal since this latter method of clinical thermometry was used unquestioned and unchallenged for a century, and yet rectal temperature actually has no thermal significance. It is far removed from the heart or the central nervous system where the temperature is regulated. It harbors intense heat producing activity of microorganisms. It is not known to contain any thermo-receptive elements. Obviously rectal temperatures deviate from tympanic temperatrue. It is the rectal temperature that is in error. Furthermore, Benzinger points out that rectal temperatures do not seem to permit early recognition of departures from typical patterns which it does not exhibit, change that could warn the anesthesiologist of oncoming fulminant hyperpyrexia.

In 1967 rectal temperatures were begun to be replaced in hypothermia during surgery with an anatomically acceptable yet very uncomfortable approach-esophageal thermometry. Prior to this hypothermia and hyperthermia induced by anesthetic or surgical procedures or by conditions in the operating rooms were largely ignored and routine monitoring was not considered essential. Unknown numbers of fatalities from fulminant hyperpyrexia were accepted undiagnosed until worldwide attention was called to the syndrome by Stephen.[3]

There was, however, no method for measuring the central temperature in man until 1959. There was no way of knowing that the rectal temperatures that were relied on were often unsteady. There was of course, the esophageal method which improved the situation, but the procedure had only limited application because of the discomfort associated with it. For the tympanic method there was until 1968 no commerically available instrumentation for practice in operating rooms, clinical wards and home.

These aspects have now changed. Testing programs are in progress at various medical centers. Moreover, the physiology of thermoregulation has finally called the physician's attention to the incredible precision and power of the human homeostatic system, to the potential diagnostic meaning of subtle changes of central control. For example an increase or decrease of central temperature as measured at the tympanic membrane of 0.01° C may result in an increase of heat loss or oxygen consumption rate by 10 percent of the basal metabolic rate.

The effect of pyrogens in extremely small amounts upon hypothalamic sensors is known to reduce the firing action of potentials of these neurons, to extinguish vital thermoregulatory responses and to produce dramatic alterations of body temperature. Aspirin was found to oppose these effects on the neuron. Chemical factors other than pyrogens, for example, female hormone during ovulation are known also to produce an elevation of temperature. Subtle alterations now measurable at the tympanum can be expected to reflect more faithfully characteristic changes of pyrogen levels and other pertinent

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factors in the course of disease, recovery or effects of treatment.

One important task of the future will be the standardization of clinical thermometry. If one method were to serve all purposes in operating rooms, hypothermia procedures, recovery rooms, intensive care units, hospital wards, then the limitations of esophageal and rectal temperatures will not be encountered in the tympanic approach.

The first applications of tympanic thermometry were focused on clinical conditions leading to serious imbalance of thermoregulation. Aside from fever, thermal stress makes body temperature depart from the norm-first by load-error. When the load is excessive, decompensation or failure occurs with heat stroke or fatal hypothermia. Induced hypothermia for surgery must be carefully monitored. In anesthesia, temperature deviates widely as the patient is deprived of his first and strongest defense against heat or cold stress—conscious intelligent behavior—while his autonomic defenses are seriously impaired. Fulminant hyperpyrexia in anesthesia leads to death by excessive production of heat and consumption of oxygen.

Patients with burns over large areas may die from leakage of heat through incessant evaporation. Infants are poor thermal risks[4] because of their large surface area exposed to thermal attack, with low capacity for absorption of gains or losses. The terminal patient develops irreversible trends of central temperature in patterns of prognostic significance.[5] In many of these situations tympanic thermometry has already produced surprising results.

The answers of the future will come from physicians and surgeons. It is tympanic thermometry that has made it possible to understand the maintenance of the norm and the meaning of deviation. From this may come a new regard for the importance of thermoregulation in clinical medicine. Well-being and performance depends vitally on thermal homeostasis.[6, 7] Our brain has developed a temperature standard of incredible precision in the set point of the human thermostat. This was recognized as far back as Issac Newton who at one time proposed to accept the body temperature of man as the standard for all measurements of temperature in physics.

L.H.N.

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The Moon Dust

The successful Apollo 11 placed experimental equipment on the moon and brought back 22 kgs of lunar material on July 24, 1969. The samples presented unique opportunities but they also presented potential problems. One was the possible contamination of the earth from the moon.

Less talked about but more real was the possibility of a black market in lunar specimens especially since it has been estimated by some news stories that each pound was worth 500 million dollars. Another possible danger was the hazard of a wild scramble for publication immediately after samples became available. Thus it was necessary to ensure receipt of the material by qualified investigators to prevent flagrant duplication of effort. Obviously to be encouraged were many different kinds of approaches to the analyses of the precious material while excessive applications or destruction of the extremely limited supply was to be avoided.

A Lunar Sample Analysis Planning team consisting of groups of highly qualified scientists was set up. A distinguished body of American scientists responded generously to qualified applicants from abroad. They then all participated in a Lunar Science Conference held in Houston, Texas January 5-8, 1970 and the results all were published in the January 30, 1970 issue of Science.[1]

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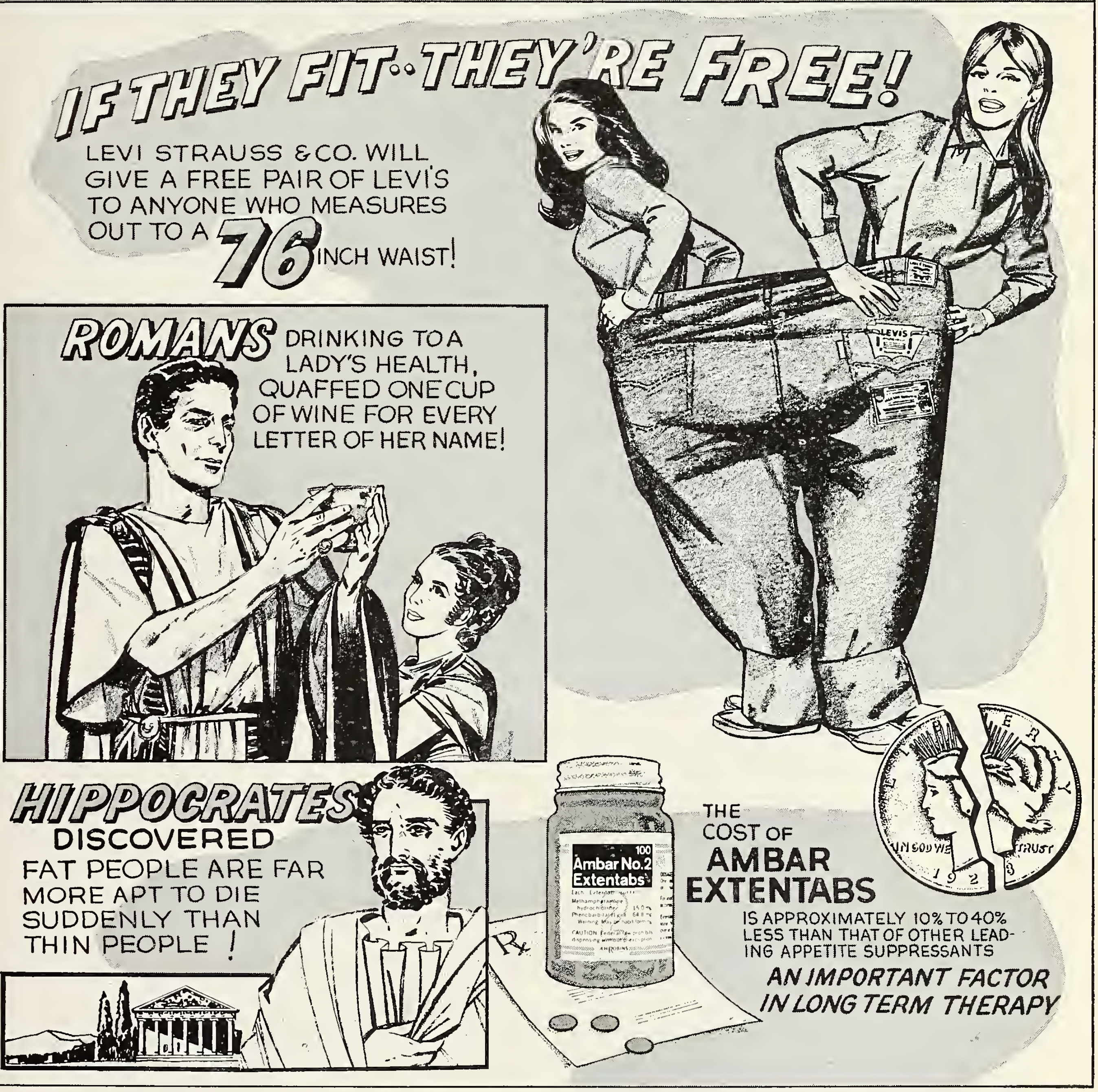

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An overview of the results of all the studies of the lunar materials are significant both for what they are and for the way in which they were achieved. The samples all came from Tranquillity Base and consist of basaltic igneous rocks, breccia which are a mechanical mixture of soil and rock fragments compacted into a coherent rock and lunar soil. The soil is a diverse mixture of crystalline fragments with a variety of fascinating shapes. It also contains small fragments of iron brought in by meteorites. In fact there was observed abundance of meteorite material in the soil. Many of the rock surfaces and individual fragments in the soil show evidence of surface erosion by high velocity impacts. There is also evidence that the impact processes are accompanied by local melting, splashing, evaporation and condensation.

There is a low abundance of many elements such as potassium, rubidium, osmium, chlorine and thallium as compared to that found in the earth, so that the moon is defective in a number of volatile elements. This permitted the scientists to infer that lunar materials had to separate from a high temperature dispersed nebula at 1000° C or higher.

What is found on the moon surface is not what can be expected of the moon interior. Nevertheless the consensus was that much of the surface of the moon is of great importance in understanding the early evolution and differentiation of planets. The material analyzed by the scientists show products of considerable geochemical and petrological evolution. It gives us a concept of the early evolutionary processes of a terrestrial planet hitherto obscured from our view.

The surface of the moon is atmosphere free and is therefore a monitor of radiation from both the galaxy and the sun. There was found evidence of low energy weakly penetrating radiation. There are samples of the gases blown off the sun in the solar winds. In this way isotopic composition and relative abundance of certain elements in the sun can now be infered from direct measurements. The cosmic ray produced nuclides show that some rocks have been on or within several centimeters of the surface for at least 10 million years and within 1-2 meters for at least 500 million years.

What was especially of interest to life scientists is whether there exist complex carbon compounds in extra-terrestrial material. This would have great significance for the origin of life both on earth and other planets. Accordingly there was an intensive search for important protobiological compounds such as purines, pyrimidines, amino acids and porphyrins, with the aid of some of the most sophisticated and sensitive analytical techniques ever devised. Nevertheless, no unambiguous identification of indigenous compounds was made even at extremely low levels of less than 10 parts per billion. The only thing scientists found were the contaminants from the exhaust from the lunar module. There is carbon in the soil but not organic compounds. The carbon is thought to be deposited from the solar winds.

An intensive search for viable organism employing a multitude of environmental and media combinations produced negative results as did, of course, the one quarantine study.

Even though the samples were collected from a tiny fraction of the moon's surface, they have given us a vast new insight into the processes that have shaped their surface. They also permitted the establishment of some significant limits as to rates and mechanisms by which this surface evolved. There is clear evidence in the chemical and petrologic observations that the surface of the moon is variable in both composition and age and the next step, therefore, is to obtain samples from the Highlands and from deeper in the lunar crust to help further to advance lunar science.

The results reported in Science do not resolve the problem of the origin of the moon. However, if the moon formed from the earth, then this separation took place prior to 4.3×10^9 years ago.

L.H.N.

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A Look Into The Future Of The Clinical Laboratory

The changing patterns of medical care are leading to new technologies. A more extensive use of modern engineering science is now needed and the outlook for the future is receiving increasing allocation by the government, industry and the University. One area of great promise is the automation of clinical laboratories. Ten years ago clinical laboratories had a battery of tests limited to 12 or so different biochemical determinations. Today, the laboratories are being called on to perform any one of 50 to 350 different types of analyses and ½ billion are being performed annually. It is likely that this number will double in the next 5 years as it has every 5 years since 1946.[1]

The one method of producing faster, cheaper, more reliable and more accurate tests is the automation of the entire clinical laboratory process from sample acquisition to computer print-out of final results on the patients chart. As an outgrowth of zonal centrifuges in virology and in vaccine production, a series of analytical centrifuges is being produced which can measure samples, add and mix reagents and read the printout of up to 50 individual tests at a time. Clinical pathologists in collaboration with industrial computer concerns are developing unique data processing systems for the clinical laboratories that use conventional methods.

As a result of new computer interfaces the number of tests that can be performed has increased three-fold while the average cost per test has decreased two-fold. A completely automated system for the bacteriology laboratory is being developed, that will be able to plant, grow, identify, and isolate bacterial species. In the interest of improving the individual analytical procedures that will ultimately be part of a totally automated system, the highly sophisticated techniques of gas-liquid chromatography for mixture separation are being coupled with the mass spectrometer for sample identification and quantification in systems which are very accurate and are capable of computer control.

The complexities involved in developing an automated instrumented system are considerable. It will have to control sample flow of various tests. It must be able to perform analyses at various rates. It must assemble the results into a simple overall profile of the patient with the most important items flagged. However, accomplishments to date are heartening and stand out in sharp contrast to the present-day operations of the average clinical laboratory.

The increasing number and complexity of tests are generating serious problems with respect to their performance and the handling and storage of data from individual patients. The reproducibility and reliability of the tests and the incidence of errors could be unacceptable. Moreover, methodology must be continuously improved while profession laboratory workers and technicians are in short supply or have inadequate training. Finally is the problem that as yet there are no universal standards of comparison of the normal with the sick individual. This is especialy important when we come to the problem of multiphasic screening.

L.H.N.

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The Papilliary-Muscle Dysfunction Syndrome

As the frequency of rheumatic valvulitis declines, papillary-muscle disease will probably be an increasing concern to the physician. Just as rheumatic mitral regurgitation is surgically curable so will some mitral regurgitation due to papillary-muscle disease also be curable. In the past there has been failure to suspect the diagnosis and therefore to apply appropriate diagnostic maneuvers. The fact is that there is a broad spectrum of papillary-muscle dysfunction ranging from a transient systolic apical murmur in the asymptomatic patient with ischemic papillary-muscle dysfunction to advanced mitral regurgitation and acute pulmonary edema in the patient with papillary-muscle rupture.

Heikkilia[1] has noted a high prevalence of mitral regurgitation after acute myocardial infarction and has described the clinical consequences of the lesion. When the infarction involves the posterior wall of the left ventricle, it invariably affects the posterior papillary-muscle, whereas when the infarction is anterior, it often spares the anterior papillary-muscle. When a systolic murmur appears after posterior wall infarction one must raise the index of suspicion that the posterior papillary-muscle has been injured and the patient must be watched for the devastating complication of a rupture with severe mitral regurgitation. There are increasing numbers of reports of successful surgical correction of this catastrophe by replacement of the mitral valve with a prosthesis.[2]

There are other causes for papillary-muscle dysfunction besides myocardial infarction. Enlargement of the left ventricle from whatever cause can displace the papillary-muscle and render the chordae tendineae too short and prevent closing of the mitral valve. So can ventricular aneurysm, or anomalous valve insertion, primary endocardial fibroelastosis and carcinoid heart disease.[3]

The papillary muscles may suffer from intrinsic abnormalities arising from many causes even trauma. However, in most cases it is due to myocardial ischemia from atherosclerosis. The papillary-muscles are particularly vulnerable to decreased coronary perfusion. During systole it is the subendocardial layers that suffer in coronary circulation and are then perfused during diastole. However, if the ventricle is distended and the arterial pressure is very low as in shock, there may be a severe interference of blood flow to the papillary-muscle even in diastole. In such a situation subendocardial ischemia can occur without involvement of the coronary arteries. This ischemia can also occur in severe left ventricular hypertrophy as well as following infusions of catecholamines. Furthermore, if there is anemia or CO poisoning then 02 delivery to the subendocarium may be impaired.[4, 5]

The diagnosis of papillary-muscle injury is not difficult. A holosystolic murmur at the apex eventually develops with progression of chronic ischemic disease, fibrosis or contraction or both. At the beginning the murmurs may wax or wane, in relation to the adequacy of papillary-muscle perfusion. If the muscle ruptures the murmur is rough holosystolic and apical and there may even develop a systolic thrill together with a fourth heart sound. As might be expected the electrocardiographic findings result from lesion usually in the posterior wall that caused the injury. The papillary-muscle as indeed the whole endocardial layers of the heart are electrically silent.

The clinical manifestations of papillary-muscle dysfunction fall into three basic types: abrupt onset with rapidly developing failure; gradual onset progressing to incapacity and failure ultimately; mild to moderate mitral regurgitation. There is a vicious cycle that can be set up if congestive failure results from papillary-muscle dysfunction. Mitral regurgitation of varying degree leads to increased ventricular volume. This further impairs coronary perfusion causing further ischemic ventricular function, further dilatation and worsening of the papillary muscle dysfunction.[5] This dysfunction was observed in 93 percent of patients dying from posterior wall infarction as compared with 41 percent of those dying from anterior infarction.

De Busk and Harrison[2] point out that surgery for dysfunction of the papillary-muscle alone is not good generally and the indications are much less clear than if there is papillary-muscle rupture. The surgeons look to left ventricular angiography to distinguish favorable cases for surgery. In the presence of poor ventricular function and those destined to die from chronic congestive heart failure or acute myocardial infarction they do not employ surgery. However, if there is severe progressive heart failure refractory to medical management after papillary-muscle rupture, then there is no alternative to surgery.

Of course, surgery for papillary-muscle disease is only palliative because of the continued presence of coronary artery disease in these patients. Generalized myocardial dysfunction obviously renders surgery inadvisable in many patients with papillary muscle dysfunction. Surgical experience is small, but it is becoming increasingly apparent that perhaps a sizable number of patients suffering from focal but strategically placed, ischemic lesions affecting the papillary-muscles can be returned to active life.

Angiographic confirmation of the diagnosis is highly desirable. Likewise coronary arteriography helps to determine the nature and extent of coronary artery disease. We may expect that medical diagnostic teams and surgical teams will work closely together in order to salvage the patients with the most acute and severe forms of the disease.

L.H.N.

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Side Effects Of Detergents

Soaps have been known for millennia. The legend has it that Roman ladies washing their clothes in the Tiber found that when the river waters were polluted by lye and animal fat, it had a remarkable cleaning power. Since then soap has been linked with pollution.

Detergents came into the market in the 1930's and proved more effective than soap. However, they were found to clog sewage systems and streams with foam. In 1965, however, this pollution problem was surmounted when angry consumers and Congressmen including Representative Henry Reuss (D.Wis.) forced the manufacturers to change the chemical composition of their product from alkyl-benzyl-sulphonate to linear alkyl sulphonate, which was more easily broken down by bacteria.

Biodegradable detergents are now the only sort one can buy.

This, however, only ended the foam problem. Detergents continue to be blamed for pollution. Lately they have been found to play a contributory role in eutrophication of waters by phosphate pollution. Sodium triphosphate makes up to 40 percent of most detergents. When poured into lakes and streams it may stimulate plant life, which takes oxygen out of the waters, thereby speeding up the natural aging process by which lakes develop into swamps and then into dry land.

Reuss's Committee, The Conservation and Natural Resources Subcommittee of the Government Operations Committee quoted the International Water Pollution Boards as recommending complete replacement of phosphorus in detergents no later than 1972. He regarded this as a conservative deadline and argued that partial replacement of phosphorus is possible now because it is already being done in Sweden.

However, it is obvious that any replacement's effects must not be worse than the phosphates themselves. David Dominick, Commissioner of the Federal Water Pollution Control Agency gave 1972 as a practical date for testing the amount of phosphorus pollution in waters and as a target date for replacement of phosphorus in detergents. What is really necessary is top priority to construction of more advanced waste treatment plants. As yet no substitute builders are available and elimination of phosphorus without any substitute builders would be equivalent to "setting back health cleanliness and sanitation standards many years."

There is another threat to the safety of consumers besides the environmental pollution by detergents. This threat derives from the newest detergent innovation—enzymes. Enzyme products are being investigated for their effect on the health of housewives and workers who produce the enzymes, by the Federal Trade Commission, the FDA and PHS. The enzymes are products of B. Subtilis which produces them as part of the digestive process. Theoretically, the enzymes attack protein stains which other detergents are not able to remove; blood, urine, meat juice, chocolate, etc. The flour-like dust of the enzymes in the air in manufacturing plants also digests the skin of makers hands and sensitizes their lungs producing an allergic reaction with asthma.

The enzymes are considered an industrial hazard by government agencies and by the detergent makers. There is, however, no such unanimity at present on the enzyme's hazard to housewives. The detergents and presoaks contain small amounts of the substance 0.3 to 1 percent and tests conducted by the FDA last spring and summer showed no adverse effects to housewives. The F.T.C., however, recently announced that it is not convinced and the agency plans to launch its own investigation soon.

Tests are currently underway by the P.H.S. to determine at what level most lungs and skin become sensitized to the enzyme, how long the process takes, what sort of reaction occurs and other related problems. We should soon hear the results of preliminary tests. After publication of these results the government agencies will be able to set a safe level of enzyme dust for plants. At high level—100 micrograms of enzyme per cubic meters of air, workers develop dermatitis and lung ailments. At lower levels, adverse reactions predominate in the lung. The Occupational Health Program of P.H.S. has tentatively recommended a level of 5 micrograms.

Enzymes have only been in use here for a year. However, they have been used much longer in Europe and have caused similar problems in Europe. Lancet raised the question in its June 14 issue 1969 and accordingly a committee from industry and government began to study enzymes. The soap and detergent makers have taken action to cut down the level of dust after an initial denial of Lancet's report. Most plants have now installed equipment to lower the dust level and industry is cooperating with government officials in setting safe levels.

The enzymes although beset with problems of safety and effectiveness are doing well on the home front. They are packed into more than half of the 800 million dollars of heavy laundry detergents sold annually and they have created a new 70-80 million market a year in presoaks.

Ironically the effectiveness of the detergents and presoaks is now being questioned by consumers groups and the F.T.C. which has begun an investigation to see if the enzyme products fulfill advertising claims. In fact Consumer Reports reviewing the product last January and the British Consumers Association, a non-profit consumer group, have also said that enzymes are not notably more effective than non-enzyme products.

L.H.N.

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A Look Into The Future Of Patient Monitoring

Instrumentation is playing an important role in the development of more adequate methods for health care. This can be seen in the automation of laboratory technique and in patient monitoring devices. The purpose of patient monitoring, of course, is to provide concentrated care in an effort to improve survival of the critically ill patient. The particular conditions which require highly specialized surveillance and treatment, include a variety of medical and surgical catastrophes such as pneumonia, drug overdosage, bleeding from a peptic or intestinal ulcer, diabetic coma, severe burns, strokes, pulmonary and peripheral emboli, pulmonary edema, serious disorders of cardiac rhythms, particularly in the early phase of myocardial infarction and the post-operative stresses incident to major surgical procedures.

Accordingly a variety of specialized intensive care facilities have been developed including trauma units, coronary care units, kidney dialysis units, post-operative intensive care wards, resuscitation units for the treatment of drug overdosage, asphyxia or poisoning. Patients in these units are maintained under intensive care for an average of three to four days. To date, it has been difficult to provide any quantitative documentation relative to an increase in survival as a result of the establishment of these units. However, there is little doubt that they have been life-saving. Probably the most significant statistical information has come from the coronary care units which have shown that the early recognition and treatment of arrhythmias in patients with acute myocardial infarction have definitely produced an increased rate of survival.

There are basically two reasons for monitoring the acutely ill patient. The first, is to provide a more frequent or where possible, continuous presentation of the patient's condition by monitoring some fundamental physiological variable. The instrumentation involved must detect trends and changes which warn that prompt treatment is needed lest some irreversible catastrophe such as cardiac arrest has occurred. The second, is that it stimulates the development of more sophisticated types of monitoring which will be designed to extend sensing capability by providing information that otherwise would not be available. To date some electronic instruments of the first type that are able to continuously and effectively monitor the basic data required, have been provided by the manufacturers. However, we are in need of semi-automatic electronic devices and it is here that the engineer has much to contribute both in the development of the instruments needed and in participation in the research studies.

Methods of patient monitoring fall into several categories. One is surveillance by hospital personnel both professional and technical who must continuously observe the patient. The second, is obtaining of conventional vital signs such as pulse rate, blood pressure, electrocardiogram, respiratory rate and temperature. The tracing of the electrocardiogram is easily retrievable and to date it has been the core of almost all electronic monitoring packages. A variety of automatic devices have been provided for blood pressure and pulse rate but they are not entirely retrievable. Respiratory rate has been followed by a variety of means including temperature sensors in the upper airway and the monitoring of chest wall movements. Usually the vital air volume which may be a more important parameter is neglected.

Measurement of central venous pressure is most important in shock. It relates to the adequate replacement of circulatory blood volume. It reflects the balance between peripheral arterial pressure and central resistance to venous return. The measurement of blood volume can be helpful in appropriate situations. Highly significant is the extent of perfusion of various parts of the body, renal, cerebral and coronary circulation. At present we measure these perfusions by symptoms and signs the patient exhibits. Objective methods are not yet highly developed and require unacceptable extensive manipulation of the critically ill patient.

We must remember that there is a limit to the information of importance that monitoring of physiological variables actually provide. For example, knowledge of flow of blood is much more important than knowledge of pressure per se. Present methods do not permit ready measurements of organ perfusion. Of course, the ideal would be an assessment of the state of the body system as a whole, but the piecemeal knowledge that must be integrated to achieve this does not now exist.

A pertinent question is why have new monitoring devices and techniques not come into wider use. One reason is that physicians are dissatisfied with monitoring the patient by such devices. Another is that many engineering problems have arisen in monitoring, even the conventional vital signs. A third reason is the limitation in the competence of medical personnel to operate complicated devices.

The engineering problems are numerous because development of an adequate patient monitoring system must include the development and validation of primary sensors. There is needed automation of measuring and controlling devices. There must be developed and tested effectors such as pumps, pacemakers and others. Then there must be developed data aquisition systems Essential is elaboration of special purpose data management techniques. There must be developed informational output procedures to condense the data into a form that can be presented to the physician and nurse in a functional fashion for decision making. Finally is the modelling of the decision making processes of physicians and nurses techniques for the exchange of information between patients monitoring units and other hospitals.

It is apparent that satisfactory patient monitoring requires reliable, easily applied sensing devices, together with suitable mathematical models of patients in jeopardy. Many of the basic engineering instrumentation and analytic techniques required are available and the beginning efforts suggest that soon a generally useful patient monitoring system will be built.

L.H.N.

References

1. Brown, J. H. V., Dickson, J. F., III: Instrumentation and the Delivery of Health Services. Science *166* 334, October 17, 1969.

Science News

Marihuana Psychosis

(Talbott, John A. and Teague, James W.: *JAMA*, 210: 299, October 13, 1969) In light of the intensive contact of man with *Cannabis* it is surprising to find the literature so lacking in regard to adverse reactions to smoking marihuana. Ames and Allentuck reported psychiatric symptoms following ingestion of marihuana concentrate, and Keeler interviewed persons who had previously had adverse reactions to smoking marihuana, but, to our knowledge, the only report describing individuals studied while experiencing adverse reactions to smoking marihuana is that of Bromberg in 1934.

Knowledge concerning the effects of *Cannabis* derivatives have been used for medicinal purposes since the third century B.C. Shen Nung, the Emperor of China, 2737 B.C., extolled *Cannabis* derivatives as healthful and as psychic liberators. During the 19th century more than 100 medical reports were published in the United States recommending the use of *Cannabis* derivatives. Although by 1950 worldwide usage was estimated in excess of 200 million persons, only recently have medical investigators begun to study the effects of smoking marihuana.

Individuals are affected by *Cannabis* derivatives on a continum ranging from a benign intoxicating "high" to a frank schizophrenic-like psychosis. Smoking marihuana for most persons is a pleasant, nonthreatening, and ego-syntonic experience. The degree of intoxication, pleasure, and mystical experience is variable and depends on the individual's personality, the existing emotional set before and in regard to the experience, and the amount of marihuana smoked or swallowed.

Adverse reactions to marihuana are also varied, but the experiences are generally unpleasant, threatening, and ego-dystonic. Symptoms include anxiety, fear, tachycardia, dyspnea, crying, depression, suspicion, dissociation, depersonalization, disorientation, confusion, paranoid ideation, delusions, and auditory hallucinations. Most adverse reactions are treated by the individual's peers in much the same manner as belligerent drunkenness is handled —with time, patience, and sobering up. However, when symptoms persist, or the individual or his peers become frightened of the behavior, medical care may be sought.—L.H.N.

Life-Threatening Infection

(Westenfelder, G. O. and Paterson, P. Y., Choice of Alternate Drugs When Penicillin Cannot Be Given, *JAMA* 210: November 3, 1969). When a patient with bacterial meningitis, bacterial endocarditis, or staphylococcal septicemia is suspected or proved to have severe penicillin allergy, treatment with an antimicrobial agent other than penicillin or one of its semisynthetic analogues may be warranted.

Chloramphenicol sodium succinate can be substituted for a penicillin in the treatment of pneumococcal, meningococcic, or *Hemophilus influenzae* meningitis. Vancomycin hydrochloride can be prescribed as an alternate drug for treatment of enterococcal endocarditis. Vancomycin or cephalothin sodium is recommended for bacterial endocarditis caused by penicillin-susceptible streptococci or for staphylococcal septicemia.

Substitutions for a penicillin should be made only if life-threatening penicillin hypersensitivity clearly is present, or as initial therapy in an emergency until time allows allergy study in a patient suspected of being penicillin-sensitive. Tube dilution susceptibility studies and in vitro tests indicating adequate blood or cerebrospinal fluid antimicrobial activity are required for optimal management.—L.H.N.

Repair Of Ductus Arteriosus Without Surgery

(*JAMA*, 210: 1385, November 24, 1969) Dr. Verner Porstmann repairs a ductus arteriosus by inserting a plug into it from catheterizing both the arterial and venous side. He has done this successfully in 53 patients whose ductus were as large as 9 mm.

The patients ranged from 5-42 years and three year follow-up shows that none of the plugs were dislodged and the patients experienced no ill effects.

The catheters are inserted into the right femoral artery and left femoral vein. Guide wires are inserted into both catheters and heparin is employed to avoid clotting. There is a loop at the end of the guide wire in the venous catheter which is maneuvered to snare the end of the wire in the arterial catheter. A conical plug is threaded over the arterial end of the catheter and fixed in place in the ductus. The plug is plastic with a steel frame. The catheter is then withdrawn through the venous side.—L.H.N.

178th ANNUAL MEETING

of the

CONNECTICUT STATE MEDICAL SOCIETY

Hartford Hilton Hotel
10 Ford Street, Hartford, Connecticut

May 12, 13, 14, 1970

COMMITTEE ON PROGRAM OF THE SCIENTIFIC ASSEMBLY

Dr. Eckhardt

William F. Eckhardt, Jr., *New Canaan, Chairman*
Paul F. McAlenney, *New Haven*
Michael J. Esposito, *Meriden*
Howard Levine, *New Britain*
Malcolm M. Ellison, *New London*

MESSAGE FROM THE PRESIDENT

Time is eternal and the common yardstick of progress. The 178th Annual Meeting of the Connecticut State Medical Society will bring into focus the many activities of the Council, officers, committees and administrative staff during the past year. All of the business of the Society will be transacted on Tuesday, May 12th, and the membership-at-large is invited and urged to participate, through the reference committee hearings, in the deliberations of the House of Delegates.

Scientific programs will be presented on Wednesday, May 13 and Thursday, May 14. Another new concept of medical education is being introduced this year; a two day mini-course on one broad general topic. The central theme will be Endocrinology, and its relationship to various aspects of medical care. The attendance at these sessions will indicate whether this type of program is appealing to the membership. The round table discussions, (learning panels), which proved to be popular last year, have been increased in number from eight to twelve.

In addition to the business and scientific sessions, there will be interesting scientific, commercial and art exhibits to visit and enjoy. The Annual Dinner to be held on Wednesday, May 13th, will provide an opportunity for us to meet our colleagues and their wives in a social atmosphere.

Truly, every member should make a special effort to attend this Annual Meeting, to keep abreast of the times—both in his Society and his practice.

Stevens J. Martin

GENERAL INFORMATION — READ CAREFULLY

Registration

The registration desk will be located on the mezzanine floor and everyone attending the meeting is requested to register. There will be no charge for registration and all members of the Society will be given a guest luncheon ticket when and only if they register.

Parking

There are ample parking facilities at the hotel and in the surrounding area. If you wish, you may drive up to the door of the hotel and an attendant will park your car for you.

Telephone

Telephone messages will be received at Hartford 249-5611.

Luncheons

Luncheons will be served in the Cities Rooms on the Mezzanine, on May 13 and May 14 and ALL MEMBERS OF THE SOCIETY REGISTERING WILL BE THE GUEST OF THE SOCIETY. PLEASE REMEMBER A LUNCHEON TICKET WILL BE GIVEN TO MEMBERS ONLY IF THEY REGISTER.

Hotel Accommodations

Persons who wish to remain overnight should make reservations not later than two weeks prior to opening date of the meeting. Reservations will be held until 6:00 P.M. on the day of arrival, unless later hour is specified. Please indicate in your letter that you are attending the Connecticut State Medical Society meeting. Your letter should be directed to the Front Office Manager, Hartford Hitlon Hotel, 10 Ford Street, Hartford, Connecticut.

Annual Dinner

The Annual Dinner will be held at the hotel on Wednesday, May 13, 1970. The social hour will be at 6:15 P.M. and the dinner at 7:00 P.M. All persons attending the dinner will be the guests of the Society at the social hour which will begin *promptly* at 6:15 P.M. and end *promptly* at 7:00 P.M. Your reservation for dinner should be sent in as soon as possible.

Program

General scientific sessions will be held on Wednesday and Thursday in the Terrace Room and Section meetings will be held in the rooms listed in the program. "Round Table Discussions" will again be held on Wednesday and Thursday mornings.

Exhibits

All the exhibits will be located in the ballroom. Physicians should take advantage of the opportunity to review "under one roof" what is new and timely by visiting the commercial and scientific exhibits.

Round Table Discussions

Members of the Society are invited and encouraged to participate in the new learning technique which was initiated last year; Round Table Discussions, or "Learning Panels". Six of these panels will be held on Wednesday, May 13 and six on Thursday, May 14th. The subject, time and place for each is published in the Program that follows. The respective "Learning Panels" will be chaired by experienced physicians who will lead their groups, of not more than 15 participants, through in-depth examination of the topics assigned. Active participation in the group discussion will be limited to members who have pre-registered. Registration forms will be mailed to members with the Program of the meeting. Members, who have not pre-registered, will be welcome to attend the panels as observers only, within the limits of available seating capacity.

ANNUAL MEETING OF THE HOUSE OF DELEGATES

Tuesday, May 12

Terrace Room Mezzanine

Presiding: Kenneth F. Brandon, *Hartford, Speaker of the House*
Frank K. Abbot, *Waterbury, Vice-Speaker of the House*

7:30 Registration of Delegates
Continental Breakfast for Delegates and Official Guests
8:30 Call to Order
OPENING SESSION
11:45 Reference Committee Hearings—Cities Rooms—Mezzanine
1:15 Luncheon—Fourth Floor Rooms
2:30 Panel Presentation—Doctors, Patients, Insurers and their Beefs—Terrace Room
Audience Participation
Open to General Membership
4:00 Call to Order—Terrace Room
FINAL SESSION
6:30 Adjournment
Reception and Dinner for Delegates and Official Guests—Cities Rooms—Mezzanine

SCIENTIFIC PROGRAM

Wednesday, May 13

8:30 REGISTRATION—Mezzanine

ROUND TABLE DISCUSSIONS

9:00—10:30 Fourth Floor in Rooms Designated

SOME PITFALLS IN INTERPRETING ELECTROCARDIOGRAMS—Room 424
Group Leader: EDGAR LICHSTEIN, *New Britain, Connecticut*

DIABETES MELLITUS—A RE-EXAMINATION—Part I—Room 420
Group Leader: LEONARD VINNICK, *Stamford, Connecticut*

THYROID PHYSIOLOGY AND FUNCTION TESTS—Room 416
Group Leader: GERARD N. BURROW, *New Haven, Connecticut*

OBESITY—A RE-EXAMINATION—Room 412
Group Leader: PHILIP FELIG, *New Haven, Connecticut*

RENAL AND ADRENAL CAUSES OF HYPERTENSION—Room 408
Group Leader: PETER M. SHUTKIN, *New Canaan, Connecticut*

NEW TESTS FOR THE EVALUATION OF HYPOTHALAMIC PITUITARY AND END ORGAN FUNCTION —Room 404
Group Leader: BRUCE F. BOWER, *Hartford, Connecticut*

10:30 INTERMISSION TO VISIT EXHIBITS

TERRACE ROOM

Moderator: SEYMOUR REICHLIN, *Hartford, Connecticut*

11:00 RECENT ADVANCES IN PITUITARY DISEASE
SEYMOUR REICHLIN, *Hartford, Connecticut; Professor and Head, Department of Medical and Pediatric Specialties, University of Connecticut School of Medicine*

11:40 DIAGNOSIS AND TREATMENT OF CUSHING'S SYNDROME
DAVID H. P. STREETEN, *Syracuse, New York; Professor of Medicine, Upstate Medical Center; Attending in Medicine, State University Hospital*

12:20 DISCUSSION—Questions and Answers

12:30 LUNCHEON—Cities Rooms
INTERMISSION TO VISIT EXHIBITS

TERRACE ROOM

Presiding: WILLIAM F. ECKHARDT, JR., *New Canaan, Connecticut*

2:00 DISORDERS OF ANDROGEN METABOLISM IN WOMEN
C. WAYNE BARDIN, *Bethesda, Maryland; Endocrinology Branch, National Cancer Institute, Bethesda; Associate Professor of Medicine, Pennsylvania State University, Hershey, Pennsylvania*

2:40 ANDROGEN METABOLISM AND THERAPY IN HYPOGONADISM
C. ALVIN PAULSEN, *Seattle, Washington; Associate Professor of Medicine, University of Washington School of Medicine; Chief, Division of Endocrinology, USPHS Hospital*

3:20 DISCUSSION—Questions and Answers

3:30 INTERMISSION TO VISIT EXHIBITS

SEYMOUR REICHLIN
Hartford, Connecticut

DAVID H. P. STREETEN
Syracuse, New York

C. WAYNE BARDIN
Bethesda, Maryland

C. ALVIN PAULSEN
Seattle, Washington

Wednesday, May 13

MEETINGS OF SECTIONS OF THE SOCIETY AND GUEST ORGANIZATIONS

SECTION ON DERMATOLOGY

2:30 Room 424

President: Neville Kirsch, *Hartford*
Secretary: Henry R. Corwin, *Norwalk*

Mast Cell Disease

D. Joseph Demis, *Albany, New York; Professor of Dermatology, Albany Medical School*

SECTION ON GASTROENTEROLOGY

3:30 Room 408

President: Vincent A. DeLuca, Jr., *Derby*
Secretary: Martin H. Floch, *Norwalk*

A New Approach to The Evaluation of Hiatus Hernia—Esophageal Manometry

Lauran D. Harris, *Boston, Massachusetts*

SECTION ON GENERAL PRACTICE

3:30 Room 404

President: Francis Gallo, *Winsted*
Secretary: Leo P. Giardi, *Hartford*

Program to be Announced

SECTION ON INTERNAL MEDICINE

3:30 Room 412

President: Frank K. Abbot, *Waterbury*
Secretary: Louis R. Mattie, *New Haven*

Program to be Announced

SECTION ON OBSTETRICS AND GYNECOLOGY

3:30 Room 416

President: G. Lawrence Austin, *Hartford*
Secretary: Peter A. Goodhue, *Stamford*

Obstetrical Vesicovaginal Fistulas—An Experience With 39 Cases in Ethiopia

Parke H. Gray, *Stamford, Connecticut*

SECTION ON OPHTHALMOLOGY

3:30 Boston-Buffalo Rooms

President: William B. Brewster, Jr., *Hartford*
Secretary: Frederick D. Williams, *Stamford*

3:30 Business Meeting

5:00 A Few Recent Highlights in Ophthalmic Surgery
Ramon Castroviejo, New York City

SECTION ON PATHOLOGY

3:30 Room 420

President: Sebastian J. Gallo, *Middletown*
Secretary: Romeo A. Vidone, *Torrington*

Viral Encephalitis in Connecticut

Gilbert B. Solitare, *New Haven, Connecticut; Associate Professor of Pathology, Yale University School of Medicine*

SECTION ON PEDIATRICS

(Hezekiah Beardsley Club)

3:30 Room 436

President: Louis Guss, *Norwich*
Secretary: Laura Grey Morgan, *Stamford*

Eradication of Rheumatic Fever: An Unfulfilled Hope

Milton Markowitz, *Hartford, Connecticut; Chairman, Department of Pediatrics, University of Connecticut Medical School. Director of Pediatrics, McCook Hospital*

Wednesday, May 13

SECTION ON PROCTOLOGY

3:30 Room 440

President: Bernard J. Kaplan, *Hartford*
Secretary: Sanford Savin, *Bridgeport*

Granulomatous Colitis in The Elderly

William A. Hoffman, *Fairfield, Connecticut; Chief, Department of Medicine and Section of Internal Medicine, Park City Hospital, Bridgeport; Associate in Medicine, Yale University School of Medicine*

Murray A. Rosenberg, *Bridgeport, Connecticut; Attending Radiologist, Park City Hospital, Bridgeport; Chief Radiologist, Out-Patient Clinic, Veterans Administration Hospital, West Haven; Assistant Clinical Professor of Radiology, Albert Einstein College of Medicine, Bronx, New York*

SECTION ON RADIOLOGY

3:30 New York-Washington Rooms

President: Julian Mandell, *New Britain*
Secretary: Robert F. Kiley, *Hartford*

Lymphangiography

Gerald Fishbone, *New Haven, Connecticut; Assistant Professor of Radiology, Yale University School of Medicine*

WOMAN'S AUXILIARY TO THE CONNECTICUT STATE MEDICAL SOCIETY TWENTY-SIXTH ANNUAL MEETING

Hartford Golf Club

134 Norwood Road, West Hartford, Connecticut

President: Mrs. James F. Jones, *Danielson*
Recording Secretary: Mrs. Gabriel A. Ingenito, *Woodbridge*
Corresponding Secretary: Mrs. Stanley J. Weigel, *Danielson*

10:00 Registration
10:30 Business Meeting
1:00 Luncheon

Guest Speaker: Mrs. Wendell F. Roller, *Monmouth, Illinois, Health Careers Chairman, Woman's Auxiliary to the American Medical Association*

Wednesday, May 13

ANNUAL DINNER OF THE SOCIETY

Hartford-Hilton Hotel

10 Ford Street, Hartford

Social Hour 6:15 P.M. Dinner 7:00 P.M.

Program

Opening Remarks

Stevens J. Martin, *Hartford*

Presiding: Morris A. Granoff, *New Haven*

Presentation of Guests and Delegates from State Medical Societies

Fifty Year Membership Awards

Harry Loring Berman, *New Haven*
Lucian Arthur Geraci, *Hamden*
Carl Clifford Harvey, *Middletown*
Claude Currie Kelly, *Hartford*
William Henry Joseph O'Brien, *New Haven*
Israel Otis, *Meriden*
Orvill Forrest Rogers, *New Haven*
Oliver Linwood Stringfield, *Stamford*
Edwin Russel Webber, *Waterbury*
Stanley B. Weld, *West Hartford*

Dinner Music

Thursday, May 14

8:30 Registration—Mezzanine

ROUND TABLE DISCUSSIONS

9:30-10:30 Fourth Floor in Rooms Designated

Some Pitfalls in The Diagnosis of Cardiac Arrhythmias—Room 424
Group Leader: Arthur O. Phinney, Jr., *Hartford, Connecticut*

Diabetes Mellitus—A Re-Examination—Part II—Room 420
Group Leader: David S. Wilcox, *Hartford, Connecticut*

Thyroid Nodules and Thyroid Carcinoma—Room 416
(A Medical versus a Surgical Approach)
Group Leaders: William F. Eckhardt, Jr., *New Canaan, Connecticut*
Malcolm M. Ellison, *New London, Connecticut*

Disorders of Calcium Metabolism—Room 412
Group Leader: Donald M. Kanter, *Stamford, Connecticut*

Some Endocrine Aspects of Male and Female Infertility—Room 408
Group Leader: Jerome J. Klein, *Norwalk, Connecticut*

Dermatological Aspects of Endocrine Disease—Room 404
Group Leader: Sidney N. Klaus, *New Haven, Connecticut*

10:30 Intermission to Visit Technical Exhibits

TERRACE ROOM

Presiding: Paul F. McAlenney, *New Haven, Connecticut*

11:00 Variations of Adolescent Development

Robert M. Blizzard, *Baltimore, Maryland; Endowood Professor of Pediatrics, Johns Hopkins University School of Medicine*

12:30 Luncheon—Cities Rooms

Intermission to Visit Exhibits

TERRACE ROOM

PROGRAM ARRANGED WITH CONNECTICUT SOCIETY OF AMERICAN BOARD SURGEONS

Presiding: Gerald O. Strauch, *Stamford*

2:00 An Internist Looks at Surgical Endocrinology

Albert Segaloff, *New Orleans, Louisiana; Attending Physician, Ochsner Foundation Hospital; Professor of Clinical Medicine, Tulane University School of Medicine*

2:45 Recent Advances in Endocrine Surgery

David M. Hume, *Richmond, Virginia; Professor of Surgery and Chairman of the Department of Surgery, Medical College of Virginia*

3:30 Discussion—Questions and Answers

Robert M. Blizzard
Baltimore, Maryland

Albert Segaloff
New Orleans, La.

David M. Hume
Richmond, Virginia

Thursday, May 14

MEETINGS OF SECTIONS OF THE SOCIETY AND GUEST ORGANIZATIONS

SECTION ON ALLERGY

3:30 Room 408

President: A. Arthur Fierberg, *Hartford*
Secretary: Edward J. Conway, *Hartford*

Wheezing As A Manifestation of Pulmonary Disease

Thomas J. Godar, *Hartford, Connecticut;Director, Pulmonary Section, St. Francis Hospital*

SECTION ON ANESTHESIA

Boston-Buffalo Rooms

President: John A. Pierce, *New Haven*
Secretary: Henry T. Bonney, *Hartford*

3:30 Annual Business Meeting

5:00 Ralph M. Tovell Memorial Lecture

Recent Progress In The Development of New Neuromuscular Blocking Agents

Richard J. Kitz, *Boston, Massachusetts; Anesthetist-in-Chief, Department of Anesthesia, Massachusetts General Hospital*

6:00 Social Hour

7:00 Dinner

SECTION ON NEUROLOGY

3:30 New York Room

President: Gilbert H. Glaser, *New Haven*
Secretary: J. William Healy, *Hartford*

L-Dopa Treatment of Parkinsonism

Gilbert H. Glaser, *New Haven, Connecticut; Professor of Neurology, Yale University School of Medicine*

Round Table Discussion will follow

SECTION ON NEUROSURGERY

3:30 Washington Room

President: Rembrandt H. Dunsmore, *Hartford*
Secretary: Robert H. Sturman, *Waterbury*

Some Newer Aspects in The Treatment of Head Injuries

William F. Collins, *New Haven, Connecticut; Professor and Chairman, Section of Neurological Surgery, Yale University School of Medicine*

SECTION ON ORTHOPEDICS

4:00

Hunt Memorial Building
230 Scarborough Street, Hartford

President: Sydney Sewall, *Hartford*
Secretary: Charles T. Flynn, Jr., *Meriden*

Total Replacement Arthroplasty of The Hip

Mark G. Lazansky, *New York City; Orthopedic Surgeon, Hospital for Joint Diseases*

SECTION ON OTOLARYNGOLOGY

3:30

Shoreham Motor Hotel
440 Asylum Street, Hartford

President: Milton L. Jennes, *Waterbury*
Secretary: Robert S. Rosnagle, *New Haven*

Antibiotic Therapy in Otolarygology

Louis Weinstein, *Boston, Massachusetts; Professor of Medicine, Tufts University School of Medicine*

Social Hour and Dinner to follow

Thursday, May 14

SECTION ON PHYSICAL MEDICINE

3:30 Rooms 412-416-420

President: Otto G. Goldkamp, *Hartford*
Secretary: Edwin L. Lytle, *Wallingford*

Rehabilitation of Patient with Cancer Related Disability

J. Herbert Dietz, Jr., *New York City; Assistant Professor of Rehabilitation Medicine, Institute of Rehabilitation Medicine, New York University Medical Center; Consultant in Rehabilitation Medicine, Memorial Hospital for Cancer and Allied Diseases.*

CONNECTICUT DISTRICT BRANCH—AMERICAN PSYCHIATRIC ASSOCIATION

3:30 Room 424

President: Paul E. Kaunitz, *Westport*
Secretary: Ellis A. Perlswig, *New Haven*

Program to be Announced

CONNECTICUT DIABETES ASSOCIATION

3:30 Room 404

President: Willem F. VanEck, *East Haven*
Secretary: James C. Hart, *Hartford*

Panel—CONNECTICUT DIABETES ASSOCIATION ACTS TO MEET INCREASING DIABETES IN CONNECTICUT

Presiding: Willem F. VanEck, *East Haven, President*

Looking Ahead in Our 21st Year
Barnett Greenhouse, *New Haven; Coordinator, C.D.A.*

Public Education and Partnership: Top Priority
Ira V. Hiscock, Sc.D., *New Haven; Chairman of the Board, C.D.A.*

Four Point Program: Education, Diagnosis, Care, Research
David S. Wilcox, *Hartford; President-Elect, C.D.A.*

New Steps in Diabetes Detection
James C. Hart, *Hartford, Secretary, C.D.A.*

State-Wide Membership: Individuals and Organizations
Philip E. Nelbach, MPH, *North Haven; Executive Director, C.D.A.*

ASSOCIATION OF MEDICAL EXAMINERS OF CONNECTICUT

12:30 Rooms 436-440

President: Samuel B. Rentsch, *Derby*
Secretary: Marcus E. Cox, *Waterbury*

12:30 Luncheon for Medical Examiners, Coroners, and Guests (Dutch Treat)
Guest Speaker: Irwin H. Lepow, *Hartford, Connecticut; Chairman, Department of Pathology, University of Connecticut School of Medicine*
Subject: Progress Report on Medicolegal Investigations Act

1:45 Business Meeting—Election of Officers

2:00 Members are invited to attend the scientific program in the Terrace Room

CONNECTICUT SOCIETY OF AMERICAN BOARD SURGEONS

President: Ira S. Goldenberg, *New Haven*
Secretary: Robert J. Williamson, *Bristol*

2:00 Terrace Room—(See General Program—Thursday 2:00 P.M.)

5:00 Social Hour

6:30 Dinner

SPECIAL NOTICE

The Section on Urology will not meet this year due to the conflict with the annual meeting of the American Urological Association being held in Philadelphia.

EXHIBITS

Space	*Organization*	*Location*
1	3M Business Product Sales	Hartford, Conn.
2	William H. Rorer, Inc.	Fort Washington, Pa.
3	The D. G. Stoughton Company	West Hartford, Conn.
4	Dynatech Products Company	Burlington, Mass.
5	Arthur W. Eade Insurance Agency	Hamden, Conn.
6	Surgeons & Physicians Supply Company	Boston, Mass.
7	Mikelk Electronics	Auburn, Mass.
8	Dictaphone Corporation	Hartford, Conn.
9	E. R. Squibb & Sons, Inc.	New York, N.Y.
10	Group Insurers, Inc.	New Haven, Conn.
11	Medical Plastics Laboratory	Gatesville, Texas
12	Dome Laboratories	West Haven, Conn.
13	The Silver Hill Foundation	New Canaan, Conn.
14	J. B. Roerig Company	New York, N.Y.
15	Merck, Sharp & Dohme	West Point, Pa.
16	The Emko Company	St. Louis, Mo.
17	Thomas A. Edison Industries	Hartford, Conn.
18	American Medical Building Guild	Madison, Wisconsin
19	Boston Medical Laboratory, Inc.	Boston, Mass.
20	University of Connecticut School of Medicine	
21	Conn. Dairy and Food Council, Inc.	Hartford
22	Starlite Farm Foundation	North Stonington, Conn.
23	Cameron-Miller Surgical Instruments Company	Chicago, Illinois
24	Parke, Davis & Company	Detroit, Michigan
25-28	Connecticut Physicians' Art Association	
29	Mead Johnson Laboratories	Evansville, Ind.
30	Eli Lilly and Company	Indianapolis, Ind.
31-34	Connecticut Physicians Art Association	
35	Lessere-Werthein, Inc.	Hartford, Conn.
36-37	Connecticut Diabetes Association— Connecticut State Department of Health	
38	University of Connecticut School of Pharmacy	
39-40	St. Francis Hospital	Hartford, Conn.
41	Woman's Auxiliary to the Connecticut State Medical Society	
42-43	Connecticut Tuberculosis and Respiratory Disease Association	
44-45	Connecticut Heart Association	
46	Maternal & Child Health Section, Connecticut State Department of Health	
47-48	Section on Ophthalmology, Connecticut State Medical Society Connecticut Society for the Prevention of Blindness	
49	Coca-Cola USA	Waltham, Mass.

THE PRESIDENT'S PAGE

Connecticuts Medicaid Melodrama

It is a well documented fact that the Medicaid program in Connecticut was characterized by a prompt, widespread acceptance immediately after it was enacted by our State Legislature in 1967, implementing Title XIX of P.L. 89-97. It is also well known that it was eminently successful in operation—receiving the full support of the Commissioner of Finance, the Commissioner of Welfare, the Professional Policy Committee of the State, the members of the Medical Advisory Committee, and the Connecticut State Medical Society. More Medicaid eligible people were seen by more practicing physicians, generalists and specialists, in our state then ever before under a federally supported program. The "usual and customary fee program" worked exceptionally well. And, to top it all off, the plan was carried out within the prescribed budget. Our Governor was gratified and the Commissioner of Welfare was elated. So successful was the plan that HEW awarded a Certificate of Merit to the State, and it was nationally heralded in the November 1969 issue of *Medical Economics*. The Medical Society of the State of New York "drooled"—they could not understand how a Medicaid program could benefit so many people, while being reasonable in cost and free of abuse.

Then came the "deluge"! Connecticut's "day of reckoning" arrived as the Democratic Party, then in power, was unable to balance the State's budget and saw fit, in their desperation, to decrease drastically the welfare budget, forsaking the care of our Medicaid brethren. Furthermore, a fixed schedule was hastily announced last March for payments of care given to Medicaid patients. Shortly thereafter, the Commissioner of Welfare and the Commissioner of Finance *resigned* to take other posts! A crisis developed. While the new Commissioners were being oriented to their tasks, the number of Medicaid patients being seen and the number of practicing physicians participating in the Medicaid program decreased markedly. In fact, one might even challenge whether the number of physicians participating in the plan now (February 23) is not below the HEW-stipulated two-thirds level to qualify for federal sharing! Only the winter, with its biting cold, prevented a protest march to our state Capitol by welfare beneficiaries.

Despite repeated afternoon and evening sessions with the new Commissioners of Finance and of Welfare since the summer of 1969, the representatives of the Society have been able to obtain only a consensus of understanding of the problems of medical care of welfare beneficiaries, but not on commitments.

During the early weeks of February of this year, however, renewed efforts were made by Doctor Charles Polivy, members of his Liaison Committee, officers of the Society and our Executive Director to get some action. It affords me pleasure and a sense of relief to be able to inform you that definite progress is being made toward revitalizing the Medicaid program in the State of Connecticut. Mind you, nothing final has been settled in establishing a flexible reimbursement formula despite the decreasing physician participation. There are indications however, as of this date, that lead me to make the following predictions:

1. Instead of a fixed fee schedule for payment of care given to Medicaid patients there will be a reasonable payment formula with a maximum for 4 different charge areas of the State. This is different from a fixed fee method.
2. The Medical Advisory Committee of Society-designated physicians for "Peer Review" will be reactivated.
3. It is expected that there will be a periodic evaluation and review of the program to reflect adjustments needed.
4. There will be more flexibility of operations in the program.
5. The administration of the Medicaid program will be coordinated under the control of a separate Health Commission, rather than the present piecemeal arrangement under the Departments of Welfare, Finance and Control.

Your President is optimistic enough to believe that the best features of our original Medicaid program will be restored and the program will once again benefit the needy and near-needy as it did in 1967-69.

STEVENS J. MARTIN, M.D.

Judges For The Connecticut Physicians' Art Association

The judges for the Art Exhibit will be: Mrs. Ethel Stauffer of Hamden, painter and teacher, past president of the New Haven Paint and Clay Club, member of the Connecticut Academy of Fine Arts and the Pennsylvania Academy of Fine Arts; Gail W. Martin of Hartford, Professor of Art at the University of Hartford, member of the Connecticut Water Color Society and the Connecticut Academy of Fine Arts; and Mitchell Pappas of Hartford, painter and Associate Professor of Fine Arts at Trinity College, Director of the Austin Art Center, member of the Connecticut Water Color Society and the Connecticut Academy of Fine Arts.

Artists — Attention!

GENERAL INFORMATION: The Connecticut Physicians' Art Association is planning the 1970 Art Exhibit in conjunction with the annual meeting of the Connecticut State Medical Society. The following information is submitted for guidance to art hobbyists.

WHERE: Hartford Hilton Hotel, Hartford, Conn.

WHEN: May 12, 13, 14, 1970

ELIGIBILITY: Physicians (members of the Connecticut State Medical Society) and their families are cordially invited to join this group of art hobbyists. (In the case of children and other members of physician's family, kindly indicate relationship to sponsor.) All previous exhibitors are invited to show their works at this meeting, white etchings, photography, pastels, collages, and new exhibitors are welcomed. Works eligible will include oil, water colors, tempora, black and mixed media and sculpture. Paintings over 24 × 30 will be hung only at the discretion of the art committee depending upon available space.

JUDGING: Art works will be judged in four categories: 1. Children under 16 years (children over 16 will be judged with adults); 2. beginners; 3. intermediates; 4. professionals. Pictures should be framed and wired for hanging. The exhibit will be judged by professional artists.

COST: A hanging fee of two dollars ($2.00) will be charged for each entry and fifty cents (50¢) for children under 16 years with two entries per artist. (Space requirements have caused our limiting the entries to two this year, as just noted.)

HOW TO APPLY: Entry blanks will be mailed to former exhibitors and also may be obtained by writing to the addresses of the committee listed below. One half of the entry blank should be submitted to me at the below address with your check prior to April 20, 1970. The other half should be attached to the picture. Make checks payable to the Connecticut Physicians' Art Association. Please fill in entry blanks completely so that entry can be categorized early in the above noted four categories.

SUBMITTING: Art works must be submitted to a representative of the Art Association in the lobby of the Hartford Hilton Hotel on Sunday, May 10, between the hours of 12 and 3 P.M. Parking temporarily near the side entrance is possible for the few minutes involved in dropping off these art works. It may be possible to aid exhibitors with the transportation of art works by contacting members of the committee noted below. These art works must be picked up on Thursday, May 14, between 12 and 4 P.M. Members of the art committee or their representatives will be in attendance at the display throughout the exhibit at the state meeting. The Connecticut State Medical Society, the hotel (nor the Art Association) can assume no responsibility for loss or damage of any cause to art works.

Under no condition can art work be accepted after MAY 10th.

If further information is needed, the following persons may be contacted:

Eugene Rightmyer, M.D., President, 114 Sherman Ave., New Haven; Mrs. Orvan Hess, Vice President, 29 Old Orchard Road, North Haven; Ann Murphy, 8 E. Normandy Drive, West Hartford, Chairman, Art Committee, Women's Auxiliary, CSMS; Mrs. John Shoukimas, 26 Pheasant Hill Dr., West Hartford; Edward Williams, M.D., 580 Hillside Ave., Naugatuck; Herman Austrian, M.D., 935 White Plains Road, Trumbull; Kurt Oster, M.D., 880 Lafayette Blvd., Bridgeport; Stewart J. Petrie, M.D., 56 Minerva St., Derby; Mrs. Mark Hayes, 163 Ridgewood Ave., North Haven; Mrs. Henry Sherwood, Penfield Hill Rd., Portland; Mrs. Clifford Wilson, 19 East Town St., Norwich; Mrs. Lowell Olson, 85 River Rd., North Haven.

Eugene Rightmyer, M.D., *President*
Connecticut Physicians' Art Association

Problems In Cadavaric Donations For Renal Transplantation

Martin Schiff, Jr. M.D., Bernard Lytton, M.D.
Robert S. Brown, M.D. and John A. Goffinet, M.D.

Renal transplantation is no longer regarded as an experimental procedure, but is rapidly emerging as an accepted method of treatment for chronic renal failure. Major problems however, primarily immunologic in character, still remain unresolved. The improvement in results has principally been due to a better understanding of the use of the immunosuppressive drugs in the control of early rejection, and in part to the development of tissue typing, resulting in better donor-recipient selection.

It is estimated that about 35,000-50,000 patients die each year in the United States from chronic renal disease, and probably at least 10,000 of these could benefit from long-term dialysis or transplantation.[1, 2] There are in Connecticut about 500-800 deaths annually as a result of chronic renal insufficiency. Unfortunately, only a small number of these patients are treated, as a great disproportion exists between patient need and treatment capability. There are at present in this state six hospitals with active hemodialysis programs, with the ability to maintain approximately 50 patients (Table 1). Expansion of the existing facilities and initiation of additional programs have been hampered by a lack of both financial resources and trained personnel.

TABLE I

PATIENT CAPACITIES OF CHRONIC HEMODIALYSIS PROGRAMS IN CONNECTICUT

West Haven VAH	15
Hartford Hospital	13
Yale-New Haven Hospital	8
St. Vincent's Hospital	6
Waterbury Hospital	4
Danbury Hospital	2

Many patients with renal failure have been maintained in reasonable health for a number of years by chronic intermittent hemodialysis. It is apparent, however, that this form of therapy is not the ultimate solution. Most patients retain some uremic symptoms and many develop progressive neuropathy. In addition, problems involving the patient's ability to remain employed, their restrictions of activity and diet, strained marital relationships, psychological difficulties, and the continuing high cost of treatment remain very much in evidence. Home hemodialysis will only alleviate some of these problems. It is therefore felt that chronic dialysis is merely the first step in the treatment of patients with terminal renal failure and that only successful renal transplantation offers many of them a reasonable hope for return to a normal life.

The supply of donor organs has been a major problem in renal transplantation. Kidneys are available from several sources (Table 2). A monozygotic twin is the ideal kidney donor since no immunologic barrier is present, but only a very small percentage of patients with renal failure have a twin capable of donating a kidney. In twins however, despite the lack of initial rejection there is a high incidence of recurrent glomerulonephritis in the transplanted kidney. More recently, the selection as donors of non-twin siblings who have inherited the same tissue antigens as the recipient, has been made possible by leukocyte typing techniques.[3-5] It is

TABLE 2

SOURCES OF DONOR KIDNEYS[7]

LIVING DONORS	57%	
Parent		26%
Sibling		18%
Volunteer		4%
Oblig, Nephrectomy		4%
Monozygotic Twin		2%
Other Relative		2%
Spouse		1%
CADAVER DONORS	43%	

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now estimated, however, that less than 25% of all patients needing a kidney transplant will actually have a suitable donor available within the family, although thus far parent or sibling donors have accounted for 44% of transplanted kidneys.[6, 7] There have been a limited number of transplants using living, non-related donors, such as spouses or prisoner volunteers, but the results of these have been no better than with cadaver donors.

Since the majority of patients dying with chronic renal failure have no available living donor, they are dependant upon cadaver sources if they are to undergo transplantation. There has been a steady improvement in both graft and patient survival with the use of cadaver kidneys, and because of this the justification for the use of living donors has been seriously questioned by some groups, in view of the moral, ethical, and psychological considerations involved.[8, 9]

Cadaver donors come primarily from the cardiac surgery and neurosurgical services; the former from patients undergoing open-heart surgery in whom cardiac rescusitation has failed but in whom perfusion and oxygenation is still maintained by a pump oxygenator; the latter, from patients dying without prolonged periods of hypotension, such as following subarachnoid hemorrhage, intracranial trauma, or with an intracranial malignancy. General conditions precluding acceptability as a cadavaric donor are outlined in Table 3.

TABLE 3

CONDITIONS PRECLUDING ACCEPTABILITY AS A CADAVARIC RENAL DONOR

1. Hypertension
2. Generalized Vascular Disease
3. Pre-Existing Renal Disease
4. Malignancy (other than intracranial)
5. Sepsis
6. Greater than 60 years of age
7. Prolonged hypotension

It has been estimated that in the United States it should be theoretically possible to supply *all* patients requiring renal transplantation with kidneys obtained from recently deceased individuals fulfilling the afore-mentioned criteria.[10] These kidneys, however, though seemingly sufficient in number, are very difficult to obtain, due to a variety of problems.

The particular nature of these problems varies to a certain extent with the specific institution and locality. The only renal transplantation program in Connecticut at the present time is at the Yale-New Haven Medical Center. Our problems have stemmed from legal difficulties, relationships with the potential donor's family and physician, and technical and geographical factors in the procurement of kidneys.

The advent of organ transplantation has given rise to new and perplexing legal problems, which have recently engendered considerable discussion.[11, 12] It is hoped that the recent adoption in Connecticut of the Uniform Anatomical Gift Act[13] will in great measure alleviate many of the obstacles to organ donation, particularly in the realm of willed donations. It is now possible for an individual to make provisions for donation of all or a part of his body upon his death by simply carrying a signed and witnessed card to this effect upon his person. These documents are available upon request at this institution, and have already been issued to a number of individuals.

Despite the adoption of the Act, kidneys from persons sustaining sudden, fatal accidents or illness and whose next of kin are not immediately accessable, remain unavailable for transplantation, as do those from homicide or suicide victims whose bodies fall under the jurisdiction of the medical examiner, coroner, or district attorney. The coroners have felt that they are unable to give permission for removal of the kidneys in these cases because of legal precedents which have been established elsewhere, in which the defense lawyers have successfully claimed that the removal of the organs from the deceased persons have contributed to their death. This policy is often carried to the extreme, in that permission cannot be obtained even in instances where victims of an assault have been in the hospital for several weeks before they ultimately died. It would seem that additional legislation is necessary to provide access to this not inconsiderable source. Since it is not necessary to remove the kidneys for transplantation until after spontaneous heartbeat and respirations have ceased, it is difficult to understand how either the time or cause of death could be questioned as being affected by organ donation.

Overcoming all of the legal barriers, however, will be helpful only if there is understanding and cooperation on the part of the potential donor's family and physician. The willed donation of one's own organs prior to death will for the present and forseeable future accomodate only a small proportion of the total number of patients awaiting renal transplantation. It is quite possible that public acceptance of willed donation of organs may not become commonplace for several generations. This, in large measure, will be dependant upon a public education program in this regard, which in our opinion, should be supported by all physicians.

The granting of permission for the donation of cadaver organs is at present the privilege of the decedant's family, and to obtain it requires a conscientious effort by the attending physician. In some respects this is similar, both legally and emotionally, to obtaining permission for a postmortem examination, which while sometimes a trying experience for all participants, is now unquestionably accepted as in the highest tradition of modern medical practice. The essential, and to some unacceptable, difference in organ donation is that such permission must necessarily be obtained prior to death. Since the kidneys must be removed and cooled within one hour after death, there is usually insufficient time unless organ donation has been discussed and agreed to by the family before death.

It is felt that permission for the use of cadaveric organs should be secured from the family by the physician responsible for the donor's care. Members of the transplant team are usualy not involved in this initial solicitation of consent, although they are available to talk to the family should any questions arise. Admittedly, this arrangement places a severe additional burden on the donor's physician, and may further complicate what usually is already an emotionally charged situation, without any apparent gain. It will be essential, however, for all physicians to assume this added responsibility if the needs of the patients with renal failure are to be met. There is no doubt that without the active participation of all physicians kidney transplantation will remain only a limited modality of therapy.

An alternate arrangement is to have another physician, who is not involved with the care of either the potential donor or recipient, or possibly a member of the clergy, obtain consent from the family. This would obviate any possible difficulties which might result from a conflict of interests.

It should be noted that the ideal donor kidneys are obtained from individuals who have sustained irreversible brain damage and whose respiratory and circulatory efforts are being maintained by mechanical means. These efforts should be continued in order to allow a brief period for perparation of the recipients and mobilization of the personnel and equipment necessary to perform the nephrectomy. As a rule, when the donor is in our own institution, 30 minutes is sufficient to accomplish this. It is essential that the kidneys be removed and cooled to 4°C within one hour after effective renal perfusion ceases.

The determination of the time of death has become a new and difficult problem due to the recent advances which have been made in maintaining the perfusion of oxygenated blood through the tissues of the body. Death must now be considered to have occurred when the patient's disease process has produced irreversible changes in the vital centers despite any of the techniques of rescusitation which may be employed.[14] It is felt that the final determination of death must depend upon the clinical judgment of the physician, who may be aided in his decision by any number of diagnostic tests, such as electrocardiography and electroencephalography, to ascertain when this point has been reached. Thus the Anatomical Gift Acts states that "The time of death shall be determined by two physicians who attend the donor at his death, or if none, two physicians who certify death, who shall use generally recognized and accepted scientific and clinical means to determine such time of death. The physicians who so certify shall not participate in the procedures for removing or transplanting a part."[13]

Therefore, in order for cadaveric renal donors to fulfill the needs of the community, physicians will not only have to obtain the necessary consent, but in addition may be forced to assume the responsibility for the determination of death. Provisions have been made at the Yale-New Haven Medical Center to lift this burden from the attending physician by making further use of the Anatomical Gift Act. A Roster of Physicians has been established to provide consultation in cases where determination of the moment of death is uncertain and potential donor participation in organ transplant programs is involved. Two of these physicians, one of whom is a membr of either the Department of Neurology or Neurosurgry, are available at all times in order to assume the responsibility for a certification of death. These consultations are of course performed without professional charge.

Once permission for organ donation has been obtained, and the certification of death has been made, the renal transplant team assumes the responsibility for removing the kidneys. We are prepared to go to any hospital in the State to accomplish this task or to arrange for transfer of the donor if this is preferred, without any additional expense to the family. We feel this decision is best made by the donor's family and physician, although it would appear that most families prefer to be spared the additional time and grief associated with another move. We are fortunate in Connecticut since most of the larger community hospitals, in which the majority of donors are likely to be found, are easily accessible to New Haven in terms of time and distance. The four to five hour period of ischemia, which most kidneys can tolerate if perfused and cooled within one hour after effective spontaneous renal perfusion has ceased, should be sufficient for kidneys to be removed at any hospital in this State, transported to New Haven, and revascularized. Our experience, and that of others,[15-17] suggests that this duration of ischemia is, in most instances, not detrimental to the ultimate success of the transplant.

The future advances in the field of tissue typing, immunosuppression and induction of immune tolerance will continue to improve the results of cadaveric kidney transplantation. These will be to little avail if we cannot solve the serious logistical, legal, and social problems associated with the procurement of suitable cadaver kidneys.

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Rheumatoid Carditis

Siegfried J. Kra, M.D. and Philip Fazzone, M.D.

Introduction

It is now well accepted that rheumatoid arthritis is a systemic disease that may affect all the organs of the body, including, the heart. It was once said that rheumatic fever licks the joints and bites the heart while rheumatoid arthritis only bites the joints. This concept has been thoroughly revised: Rheumatoid arthritis also bites the heart. It has been estimated that 40 to 60% of patients with rheumatoid arthritis show evidence of adhesive pericarditis at autopsy. However, pericarditis is very rarely noted clinically.[1-5] We wish to report such a case.

Case Report

A 40-year-old female, whom we saw for the first time in 1966, complained of pain and swelling of her hands and feet of six week's duration together with mild chest pain. The patient experienced 3-hour stiffness in the morning with marked swelling of both wrists and the PIP joints of both hands with some relief after taking aspirin. She also noted nodules on the dorsum of her arm. She had no antecedent streptococcal infections and enjoyed good health prior to this episode. She denied sunlight sensitivity, urethritis, or conjunctivitis and had no psoriasis.

Her family history was unremarkable except that her sister had rheumatic heart disease.

Physical examination disclosed a well-developed, young woman with some discomfort. Her blood pressure was 130/70 in the left arm and 130/75 in the right arm. Pulse was 75 and regular; temperature was 98.6. No skin rash was evident except for the subcutaneous nodules on her arm. Pertinent physical findings were limited to the musculoskeletal and the cardiovascular systems.

Examination of the hands disclosed bilateral fusiform swelling of the 3rd and 4th proximal interphalangeal joints. She had swelling of her wrists and tenderness of the synovium with pain on flexion and extension of the PIP joints of the wrists and fingers. Her elbows were swollen and subcutaneous nodules occurred on the dorsal surface. The patient experienced some pain on flexion of both arms but motion was unlimited.

Examination of the cardiovascular system revealed the following: flat neck veins, small A waves, blood pressure: 130/75 in the left arm, paradoxial pulse: 5 millimeters, and of no pulsus alternans. Auscultation of the heart disclosed normal splitting of the second heart sound and an atrial sound, but no third heart sound. Over the entire sternum was a loud to and fro coarse friction rub, maximum on inspiration and radiating to the apical area. Heart sounds were somewhat distant. No murmurs were heard. No hepato-jugular reflex was present. An electrocardiogram disclosed symmetrical inversion of T waves over the precordium, compatible with pericarditis. X-ray of the chest showed minimal cardiomegaly.

Laboratory examination revealed the following findings: White blood count: 7,000 with a normal differential count, sedimentation rate: 50 mm/1 hr (according to Wintrobe method); hematocrit: 43% homoglobin: 14.25 grams; serum uric acid: 4.0; serum calcium, phosphorous, and electrophoreses; normal. ASLO Titer: normal; numerous Lupus preparations: normal; rheumatoid factor test: positive 1/320 dilutions using the Standard Hyland Latex Test. Liver function tests, cephalin flocculation, thymal turbidity, and alkaline phosphotase were within normal limits. Skin tests for Tuberculosis and fungi were negative.

We concluded that the patient was suffering from rheumatoid arthritis with pericarditis. She was started on a course of 12 to 18 aspirins per day. Her arthritis symptoms were markedly relieved, the pains in her fingers and swelling of her wrists decreased but the morning stiffness persisted. The pericardial friction rub remained but the patient was not in respiratory distress nor did she have chest pain.

After approximately three months of treatment, the patient experienced severe chest pain which increased on inspiration and was associated with diaphoresis. She was admitted to Yale-New Haven Hospital. Physical examination disclosed a female in acute distress and dyspneic. Blood pressure was 140/80 in the left arm; pulse was 120 and regular. Large A waves were present in the neck and the veins were distended. A loud to and fro precordial friction rub, a loud atrial sound and a definite third heart sound was heard. Examination of the lungs disclosed rales up to the apices.

We believe the patient was in left-sided heart failure. Chest X-ray disclosed marked prominence of the left ventricle as well as a diffuse irregular infiltration throughout both lung fields. Treatment was started for pancarditis; the patient received 60 mg. Prednisone per day and was digitalized. Her symptoms subsided during the next 24 hours. She was no longer in heart failure and her chest X-ray cleared completely. Studies for lupus preparations and anti-nuclear tests were negative, as well as repeat studies for fungi and tuberculosis. The rheumatoid factor test was positive in 1/1440 dilutions. The patient was maintained on 15mg of Prednisone per day and Digoxin 0.25 mg. q.d. until October of 1967 when she discontinued Prednisone and again experienced severe chest pain and shortness of breath. She was admitted to the Hospital of St. Raphael. Examination again disclosed a loud friction

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rub and congestive heart failure. She was given 60 mg. of Prednisone and her symptoms disappeared in 24 hours.

At this time, a right heart catherization was performed. An angiogram revealed a significantly elevated pulmonary capillary pressure of 40/20, and right ventricular pressure of 40/12. Neither paradoxical venous pulse nor pericardial thickening were evident.

Because mitral valve disease was absent, we concluded that the elevated pulmonary capillary pressure was caused by loss of left ventricular compliance. Absence of pericardial thickening of significant pericardial fluid indicated that the loss of compliance was due to myocardial pericardial tamponade. Thus, the patient showed evidence of pericarditis and myocarditis which we concluded was rheumatoid in origin.

As soon as, the patient received Prednisone in adequate dosage, her symptoms promptly subsided even before the full digitalization dosage had been completed. The patient is presently comfortable and asymptomatic, receiving Prednisone, 5 mg. t.i.d. and digoxin, 0.25 mg. every day.

Comment

The gross disparity between the lack of clinical findings of heart disease in peripheral rheumatoid arthritis and the anatomical findings is well known. Pericarditis is rarely diagnosed clinically with rheumatoid arthritis except in juvenile arthritis of Still's Disease.[6] Yet as many as 50 to 60% of autopsies have demonstrated association between the two diseases.[7]

Rheumatoid nodules have been found in the epicardium and the myocardium in the rings and leaflets of mitral and aortic valves. Mitral valvulitis has been described in a study of 1150 rheumatoid patients at Bellevue; 40.6% cases of pericarditis revealed pericardial infiltration as well as adhesive and healed pericarditis. According to this study made by Sokolov, patients with rheumatoid arthritis showed more than 17 times the evidence of healed idiopathic pericarditis than other individuals. Granulomatous pericarditis may also occur in these patients. It has been speculated that these cases represent burnt-out pericarditis. Likewise, granulomatous lesions are frequently found in the myocardium. These findings have been considered specific for the diagnosis of rheumatoid heart disease. The relationship between rheumatoid spondylitis and aortic insufficiency is well documented. In a very recent report by Schwartz,[9] which described a patient with rheumatoid carditis in heart failure, an autopsy revealed granulomas throughout the myocardium. Lieberwitz[10] studied the myocardia of patients with rheumatoid arthritis. The mean age of the patients was 47 years. Sixty-two of these patients showed evidence of having had pericarditis at one time. It has been estimated that 1 to 3% of autopsied patients with rheumatic disease have granulomas in the heart.

Why do not more patients with rheumatoid arthritis present with clinical manifestations of carditis? Many during their acute rheumatoid process, have received corticosteroids which conceivably have supressed the clinical manifestations of pericarditis. When such a patient is seen in acute congestive heart failure, an underlying rheumatoid etiology should be sought, as the picture of heart failure can be dramatically reversed by steroid therapy. It is hoped that this report will alert more attention to perhaps a not uncommon and reversible problem.

Addendum

We had the opportunity of studying another patient with early rheumatoid arthritis and cardiomegaly. Cardiac catherization was negative, but an angiogram disclosed a pericardial effusion. The cardiac silhouette returned to normal after a 2 week course of 40 mg of Prednisone.

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Acute Organic Psychosis Due To Talwin (Pentazocine)

Murray A. Yost, Jr., M.D. and F. Patrick McKegney, M.D.

Talwin (Pentazocine Hydrochloride) is a relatively new analgesic, widely used because it has no "significant abuse liability".[1] However, a recent report describes two patients who developed tolerance to the drug and suffered a wihdrawal syndrome after its discontinuation.[2] Talwin's side effects include tremulousness[3] and it has been rarely noted to cause "agitation" and "hallucinations,"[4, 5] but a major psychotic reaction to the drug has not been described. In the following case, Talwin was the probable cause of a severe organic psychosis.

The patient, a 25 year old, white, male, was transferred to the Yale-New Haven Hospital on 3/28/69 with a diagnosis of acute candida albicans endocarditis, with aortic valve involvement. Two months prior to transfer, he was admitted to another hospital with a one month history of progressive malaise, dyspnea, chest pain, and fever. The patient was a known narcotic addict, using I.V. cocaine daily for several years prior to the onset of his symptoms. On physical examination at transfer, he was a wasted young man in moderate physical distress. Temperature 100.6 (R), BP 130/50, R 30. There were 2/6 systolic and 5/6 diastolic murmurs over the aortic area, an S_3 gallop, pounding "pistol shot" pulses, and dyspnea at rest. The lungs were clear. He had a clear sensorium, a fine tremor of the hands, and expressed anxiety about his medical condition. On transfer to Yale-New Haven Hospital for cardiac surgery, his medications included: Amphotericin 60 mgs. I.V. q.d., digoxin, 0.25 mgs. q.d., and Talwin, 50 mgs. I.V. q4h, p.r.n. for chest pain.

While being prepared for open heart surgery, the patient received many medications, including doses of Talwin averaging 130 mgs. per day for chest pain. On the 11th hospital day, his aortic valve was replaced with 6 hour 35 minute anesthesia time and 6 hour 20 minute pump time. The post-operative course was uneventful, except for a low grade fever lasting 3 days and severe chest pain, requiring high doses of Talwin. He was returned to the medical floor from the ICU on the 4th post operative day. His sensorium remained clear until the 6th post-op. day, when he was noted to be increasingly tremulous and slightly confused, especially at night. Because of sleeplessness and other signs of depression, he was begun on amytriptyline (Elavil) 25 mgs., t.i.d. His confusion and tremor worsened and by the 12th post-op. day, he began experiencing occasional auditory and visual illusory and hallucinatory phenomenon, for which perphenazine (Trilafon). 4 mgs. and benztropine mesylate (Cogentin) .5 mgs. were given q.i.d. At this time, the patient was receiving an average daily dose of 230 mgs. of Talwin. (See Figure 1). On the 14th post.-op. day, his tremulousness, confusion, and hallucinations had become so severe that the Talwin was not given, on the basis of a likely diagnosis of an acute toxic psychosis, possibly drug related. At this time he was afebrile, and without evidence of cardiac failure or aortic value regurgitation. Electrolytes, BUN, liver function tests, urinalysis, LP and C.B.C. were normal. He became disoriented in all spheres, developed paranoid ideation and formications, and all other symptoms worsened. On the 15th post-op. day, the Elavil, Trilafon and Cogentin were withheld.

The patient was unchanged on the 16th post-op. day, but on the 17th, his symptoms and signs were greatly improved and they completely resolved over the 18th and 19th post-op. days. After his recovery, the patient had vivid memories of his "lost weekend", describing the hallucinations as a "bad dream" or "nightmare." In taking distance from these events, he was able to recall the gradual onset of his confusion and hallucinations and the acute psychotic episode.

Factors possibly responsible for the psychosis, other than Talwin, must be considered. An "atropine-like" psychosis from the anticholinergic psychotropic drugs is unlikely, since the initial confusion and tremulousness preceeded the Elavil and the hallucinations occurred before the Trilafon and Cogentin were begun. However, that these drugs may have contributed to the severity of the reaction can not be ruled out. There were no other changes in his drug regimen or physical status prior to the psychotic episode. The well known post-cardiac surgery psychosis[6] usually occurs earlier, within the first three or four post-operative days and most often in the intensive care setting. An acute schizophrenic reaction is unlikely because of the rapid recovery and the patient's ability to take distance from his psychosis once it had resolved. Thus, it seems likely that in this case, the use of Talwin in high doses and over a long period of time, was responsible for the serious complication of an acute toxic psychosis. Physicians should be alert to slight

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DR. F. PATRICK McKEGNEY, Associate Professor of Psychiatry and Medicine, Yale University School of Medicine and Chief, Psychiatric Consultation-Liaison Service, Yale-New Haven Hospital.

or progressive confusion and agitation in patients receiving this drug. As with other agents which cause delirium, this complication can be reversed by decreasing or discontinuing the drug.

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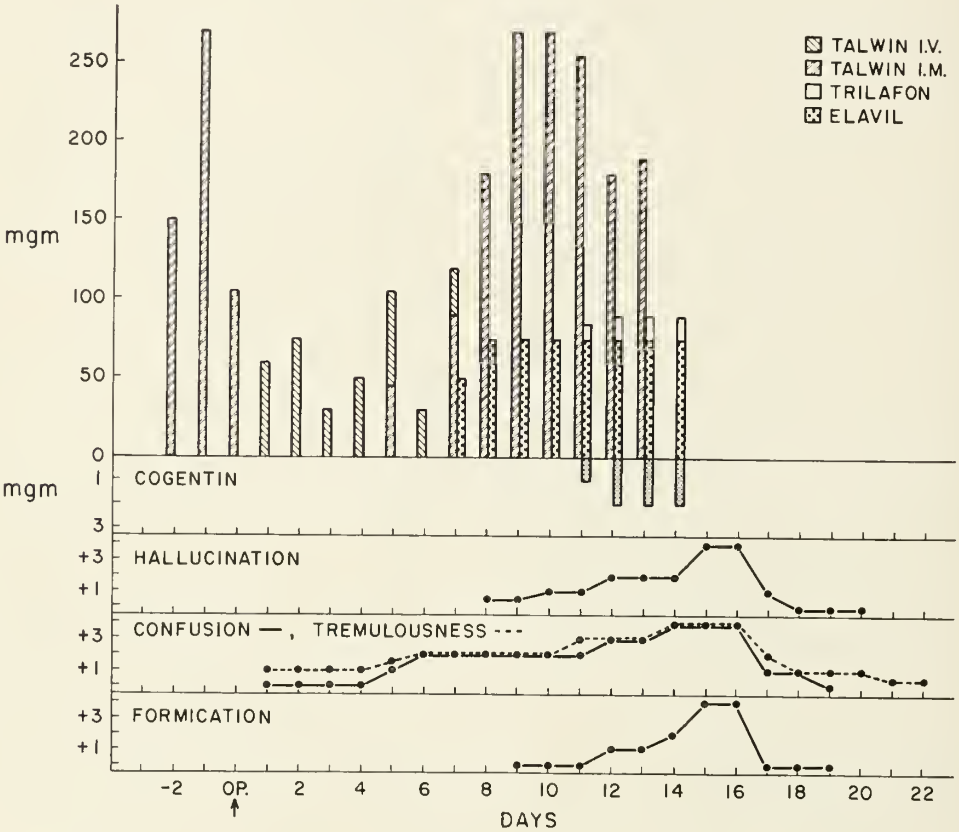
FIGURE I



Jejunal Hematoma, Child Abuse, and Felson's Sign

Marcel Bratu, M.D., John C. Dower, M.D.,
Bernard Siegel, M.D., and Salah H. Hosney, M.D.

Recent recognition of the magnitude of the problem of child abuse has broadened the clinical spectrum of the syndrome. Caffey[1] stressed the radiographic features of the skeletal lesions of trauma in growing bones and Gilespie[2] described a group of children abused by caustic or thermal agents. Blunt trauma to the abdomen during child battering has resulted in intestinal obstruction secondary to intramural hematoma of the jejunum.[3] We have recently encountered a similar patient and propose to report our experience and review the literature to alert physicians to this complication of blunt abdominal injury.

Case Description

The patient was a 22-month-old Negro female admitted to the Hospital of St. Raphael with continous bile stained vomiting which started one day prior to admission and increased in frequency during the subsequent twelve hours. Prior to admission the girl became unresponsive and somnolent. No bowel movements were noted in the previous twenty-four hours.

The social history was pertinent in that the mother worked during the day and the patient and her two older siblings were placed with a variety of baby-sitters.

On physical examination, the child was a severely dehydrated, lethargic Negro child weighing twenty pounds. She vomited bile stained material almost continuously. The abdomen was scaphoid and bowel sounds were absent. There was a slightly mobile mass in the epigastric area measuring 4 x 2 centimeters with the longer axis in the horizontal position. The remainder of the physical examination was unremarkable.

Laboratory investigation revealed the following: $Na+$ 137 mEq/L; $K+$ 4.7 mEq/L; $Cl—$ 77 mEq/L; CO_2 Combining Power 29.0 mm. Hg.; BUN 165 mg. per 100 ml.; blood sugar 132 mg. per 100 ml. The serum calcium, phosphorus and amylase were within normal limits. The urinalysis showed no abnormalities.

A roentgenogram of the abdomen taken immediately after admission (fig. 1) was interpreted as showing a moderately dilated stomach and duodenal cap. There was persistent narrowing in the proximal jejunum.

The following day a barium contrast study of the small bowel confirmed the narrowing of the jejunal lumen just distal to the ligament of Treitz (fig. 2). The appearance was reminiscent of the "coiled spring" appearance reported in duodenal intramural hematoma by Felson.[4]

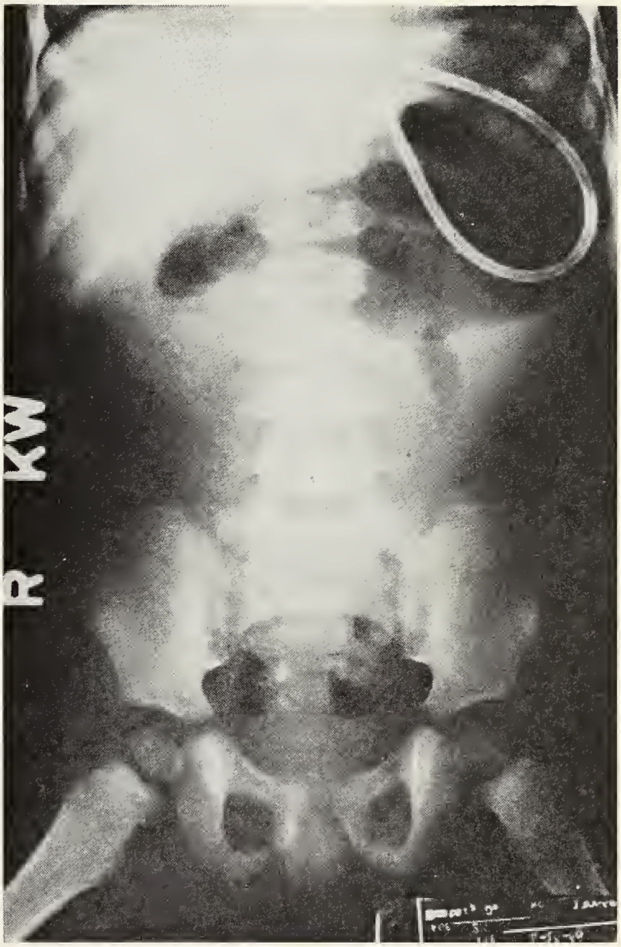


Figure 1
Film of the abdomen showing dilatation of the stomach and duodenum. Persistent narrowing of the proximal jejunum is evident posterior to the air filled stomach.

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DR. JOHN C. DOWER, Professor of Community Pediatrics, Department of Pediatrics, Children's Hospital of Buffalo, Buffalo, New York.

DR. BERNARD SIEGEL, Assistant Attending Surgeon, Department of Surgery, Hospital of St. Raphael, New Haven, Connecticut.

DR. SALAH H. HOSNEY, Surgeon, Washington Hospital Center, Washington, D.C.

Correction of the dehydration and metabolic alkalosis was started and because of persistence of high intestinal obstruction, an operation was undertaken on the third hospital day. With the patient anesthetized, the epigastric mass could be easily palpated and on opening the abdomen, clots of fresh blood were found. The loop of jejunum distal to the ligament of Treitz was delivered into the wound and a subserosal hematoma about three inches in length partially encircling the entire circumference of the jejunum was noted. Following a serosal incision, this was evacuated. There was profuse oozing of blood from the serosal surface of the jejunum which was stopped by compression with saline packs. The serosa was resutured and the abdomen closed. The post-operative course was uneventful.

When the mother was confronted with the probability that the lesion was traumatic in origin, she confessed that the child had been admitted to another local hospital twice within the previous six months because of soft tissue lesions sustained during physical abuse. The child was placed in a foster home following hospital discharge.

Review of Previous Reports

In spite of recent publicity in the lay and medical press regarding the prevalence of child abuse, the magnitude of the problem, the protean clinical manifestations, and the natural history and epidemiology of this disease are not sufficiently appreciated.[5] Kempe[6] collected 302 cases of child abuse over the period of a one year survey of 77 hospitals. In this group, 32 deaths and 85 cases of permanent brain damage resulted. We have been particularly impressed with the repetitive nature of the traumatic episodes. Many of the deaths are preventable if initial child abuse episodes are detected and appropriate action taken. The psycho-social setting of child battering has been reviewed by Wooley[7] and Cohen.[8] From these and similar studies, the chronicity and episodic nature of this entity are often predictable.

Intramural hematoma of the jejunum is rare in children and it is generally accepted that the susceptibility of the duodenum to intramural hematoma following trauma is due to its fixation as it passes over the vertebral bodies. Although the intestine is a hollow organ, blunt trauma delivered to

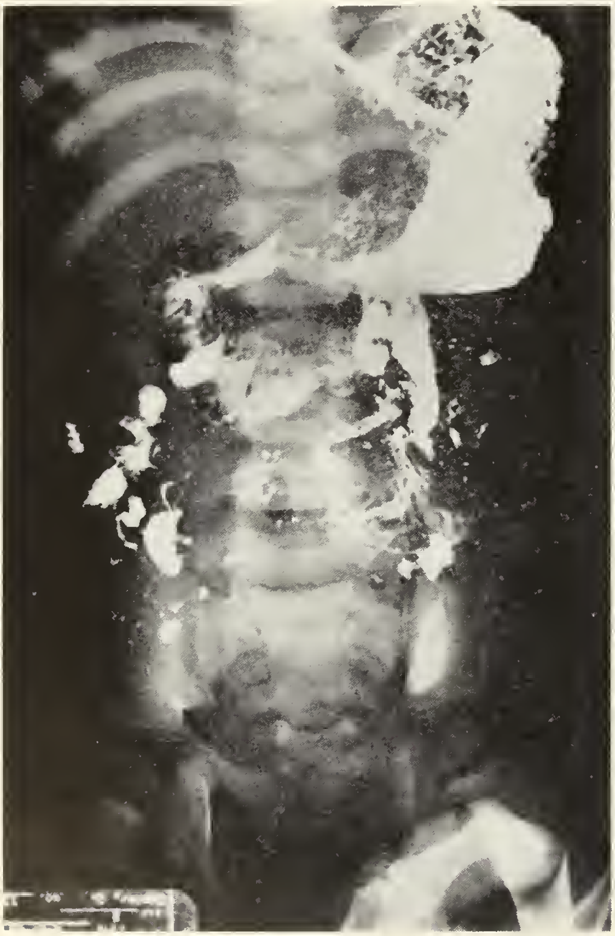
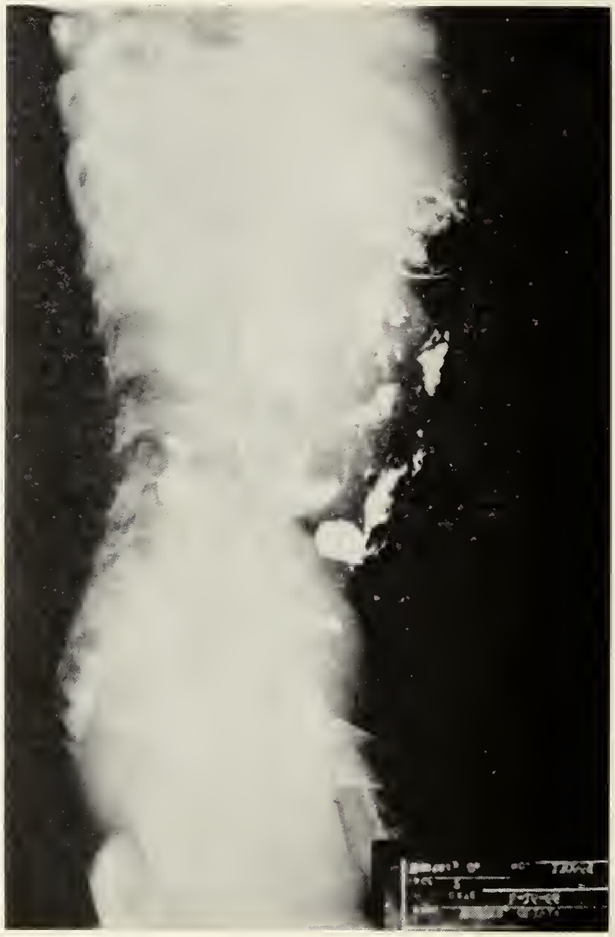


Figure 2

A: Barium contrast study (AP View) showing mucosal irregularity, narrowing of the proximal jejunal lumen, and the "coiled spring" sign of Felson.



B: Lateral view showing the contrast material outlining the intramural hematoma cavity.

a fixed portion can result in subserosal hemorrhage.[9, 10]

Judd[11] reported a 28-month-old child with a duodenal-jejunal hematoma. He reviewed the literature and described 75 patients with intramural small bowel hematomata which were traumatic and 75% of the latter were in children under fifteen years of age. Bailey[12] and Moody[13] described similar patients and noted blunt trauma, steering wheel injuries, bicycle accidents, and body contact sports as the usual insults. Eisenstein[3] described the first patient with small bowel hematoma resulting from child abuse. The child described in the present report probably represents the second such patient. We are convinced that there are a significant number of unrecognized similarly traumatized children.

While the number of patients is too small to justify sweeping conclusions, an analysis of the literature suggest the following characteristics (Table 1).

Age

Sixty-one per cent of the patients were in the school age group, a period characterized by vigorous physical activity. Five patients have been reported under six years of age. One patient was a newborn with probable iatrogenic hematoma (an infant with a tracheo-esophageal fistula with possible jejunal trauma during operation). Of the remaining four patients, two were battered children.

Sex

There is a striking predominance of males, which probably reflects more vigorous play. Again in spite of the small numbers, the sex of the patient has little bearing on incidence if children approximately two years of age are considered.

Signs and Symptoms

Vomiting is the chief symptom due to intraluminal obstruction by the intramural hematoma. The vomiting may be bile stained and constipation is common. These symptoms reflect high intestinal obstruction which is frequently complicated by rapid and severe dehydration associated with hypochloremia and metabolic alkalosis. Abdominal pain was noted frequently in older children. An abdominal mass was found in more than 50% of the patients.

Radiographic Findings

Felson[4] first described the "coiled spring pattern" in duodenal hematoma and observed: "From the pathological description in the literature, it is probably that similar roentgen changes would also be encountered in intramural hematomas involving other portions of the small intestine. Unfortunately, roentgen descriptions are not available in such cases." Since that report, Bruck[14] and Culver[15] described similar findings in intramural jejunal hematoma.

An explanation for the radiographic appearance relates the trauma to compression of the fixed retroperitoneal portions of the duodenum or jejunum against the spine. Disruption of the mesenteric attachment in this region initiates the hemorrhage and the resulting intramural hematoma separates the serosa from the muscularis. The mass bulges into the lumen giving rise to radiographic evidence of an intramural mass. The resulting edema or hemorrhage into the mucosa causes thickening and obstruction.

In the previously reported hematomata in children, Felson's sign was not described. The patient reported demonstrated this characteristic sign.

Diagnosis

The infrequency of intramural jejunal hematomas in children often leads to erroneous diagnoses such as acute appendicitis, peritonitis, volvulus and intussusception. In only a few patients reported has the preoperative diagnosis been orrect. The severity of the abdominal trauma bears little relationship to the occurrence of intramural

TABLE 1

CLINICAL FEATURES OF JEJUNAL HEMATOMA

Age	*Sex*		*Symptoms*			*Diagnosis*			*Treatment*		
	M	*F*	*ABD. Pains*	*Vomiting*	*Mass*	*Corr.*	*Incorr.*	*Suspect*	*Evac.*	*Res.*	*Cons.*
0-4	2	2	1	3	3	—	2	2	2	1	—
4-6	1		1	1		—	1	—	—	1	—
6-16	8		8	8	5	4	3	1	1	—	1
Total	11	2	10	12	8	4	6	3	9	2	1
Percent	84%	16%	77%	92%	60%	30.5%	46%	23%	69%	16%	8%

hematoma and relatively minor episodes have produced the lesions. The time between trauma and appearance of symptoms is usually three to four days.

Treatment

Treatment has usually been conservative consisting of evacuation of the hematoma but non-operative observation is possible if intestinal obstruction spontaneously resolves. Fatalities related directly to the hematoma have not been reported in children.

Summary

A 22-month-old patient with intramural jejunal hematoma related to traumatic abuse has been reported and previous reports of similar patients reviewed. Physicians should be aware of this unusual complication of trauma especialy associated with the Battered Child Syndrome.

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PLAN TO ATTEND

ARRANGE YOUR SCHEDULE NOW AND PLAN TO ATTEND THE 178th CSMS ANNUAL MEETING TO BE HELD AT THE HARTFORD HILTON HOTEL, HARTFORD — MAY 12, 13, 14, 1970

FROM THE EXECUTIVE DIRECTOR'S OFFICE

William R. Richards, M.D.
Executive Director

160 St. Ronan Street, New Haven, Conn. 06511
Telephone 865-0587

Josephine P. Lindquist
Associate Executive Director

CALL

ANNUAL MEETING OF THE HOUSE OF DELEGATES

The 1970 Annual Meeting of the House of Delegates will be held in the Terrace Room of the Hartford Hilton Hotel, Hartford. The first session of the House of Delegates will commence at 8:30 o'clock in the morning of Tuesday, May 12, with reference committee hearings at 11:45, followed by luncheon. A special program will be held at 2:30 P.M. and the House will reconvene at 4:00 P.M. for the completion of business.

Stevens J. Martin, President
Kenneth F. Brandon, Speaker of the House
Reginald C. Edson, Secretary

INTRODUCTION OF RESOLUTIONS

Article V, Section 12, Par. 3 of the Bylaws of the Society Provides that:

All resolutions to be considered as regular business at any regular meeting of the House of Delegates must be in the hands of the Speaker not later than seventy-two hours before the opening of that meeting. All resolutions and recommendations published in the official agenda distributed to the members of the House prior to the meeting at which action is to be taken shall be considered as regular business. Resolutions presented later than seventy-two hours before the opening of a meeting will be referred for consideration as regular business by the House only when they are presented by the Council or accepted for consideration by majority vote of the delegates present. Any resolution which does not qualify in accordance with the aforesaid provisions for consideration as regular business may be accepted for action by a majority vote of the delegates present and, if so accepted, shall be referred at once by the Speaker to a reference committee. Any such reference committee shall consider resolutions referred to it and shall report, with recommendations to the House before adjournment of the meeting.

PROPOSED AMENDMENTS TO THE BYLAWS

The following proposed amendments to the Bylaws were presented to the House of Delegates on December 11, 1969 and were tabled for consideration and action at the next regular meeting of the House of Delegates.

In accordance with the Bylaws, these amendments will be published in Connecticut Medicine, "on one or more occasions prior to the next meeting . . . at which meeting the amendment shall be taken off the table and acted upon by the House of Delegates."

Introduced by the Council

I. COMMITTEE ON STATE LEGISLATION

Purpose: To reorganize the Committee on State Legislation to facilitate primary study of bills by experts in the various fields who are on the committee, rather than referring bills for study to other committees.

Amendment

ARTICLE XI—Divisional Boards and Committees

Section 5—Duties of Standing Committees

Par. 8. The Council annually shall nominate to the House of Delegates a Committee on State Legislation to consist of not less than sixteen members, including at least one member from each county, and shall nominate the chairman thereof. The members, insofar as feasible, shall be capable of representing the various speciality divisions of medicine. The functions of the committee shall be to study and review proposed state legislation. . . .

Present Bylaw

Par. 8. Committee on State Legislation. Annually before the fifteenth of January, each component association shall send to the Executive Director of The Society its nomination of an Active Member of The Society to membership on the Committee on State Legislation. The Council annually shall transmit these nominations to the House of Delegates and, in addition to these eight nominees, the Council shall nominate to membership on the Committee the Delegates to the American Medical Association and shall nominate the chairman of the committee. The function of the committee shall be study and review proposed state legislation. . . .

II. LIFE MEMBERSHIP

Purpose: To include in the Bylaws the action voted by the Council that Life Members may be exempt from the payment of dues on January 1 following their 65th birthday.

Amendment

ARTICLE IV—Membership

Section 4—Life Membership (Add the following sentence)

Exemption from payment of dues for Life Members shall become effective on January 1 of the year following the thirty-fifth year of membership or of the anniversary year of their sixty-fifth birthday, whichever is applicable.

III. ELECTION OF PRESIDENT-ELECT AND OTHER GENERAL OFFICERS

Purpose: To remove the necessity of election of officers by ballot and leaving the choice of method of election to the House of Delegates.

Amendment

ARTICLE VI—General Officers

Section 3—Term of President-Elect (Delete the underlined words)

The President-Elect shall be elected annually by ballot by the House of Delegates ....

Section 4—Terms of General Officers (Delete the underlined words)

Par. 1. Election. The Vice-President, the Secretary, Treasurer, and the Speaker and Vice-Speaker of the House of Delegates shall be elected annually by ballot by the House of Delegates..................

The House of Delegates shall elect by ballot Delegates and Alternate Delegates.. ....

IV. VACANCIES

Purpose: To provide for filling of a vacancy in the office of Vice-President.

Amendment

ARTICLE VI—General Officers

Section 4—Vacancies. (Add the underlined words)

Par. 2. In the event of a vacancy in the office of Vice-President, Secretary, Treasurer or Vice-Speaker or Delegate or Alternate Delegate to the American Medical Association, the Council shall fill the vacancy........................

V. DUTIES OF THE PRESIDENT

Purpose: To delete the statement that the President preside at all meetings.

Amendment

ARTICLE VI—General Officers

Section 8—Duties of the President. (Delete the underlined words and add words in capitals)

The President shall preside at all meetings of the Society. He THE PRESIDENT shall be an ex-officio member of all committees. He shall appoint all committees not otherwise provided for in these Bylaws, subject to confirmation by the Council ....

VI. POWERS AND DUTIES OF THE COUNCIL

Purpose: To provide for the Council to employ necessary legal counsel without directives from the House of Delegates.

Amendment

ARTICLE VII—The Council

Section 1—Powers and Duties

Par. 11. Counsel. (Delete underlined words and add words in capitals)

The Council shall employ legal counsel and or a legislative agent subject to the directives of the House of Delegates AS NECESSARY IN THE PERFORMANCE OF ITS DUTIES.

VII. DUTIES OF THE EXECUTIVE DIRECTOR

Purpose: To delete the words "Clinical Congress", which is no longer a mandatory annual meeting, and to clarify the duty of the Executive Director to keep records of CSMS committee meetings.

Amendment

ARTICLE VII—The Council

Section 3—Executive Director

Par. 2. Duties (Substitute the following paragraph)

Sub-Par. (g) To record attendance and proceedings of all meetings of the House of Delegates, the Council, and other official meetings of The Society and to maintain records of all meetings of committees of The Society.

Present Bylaw

Sub-Par. (g) To record attendance and proceedings and maintain records of all meetings of the House of Delegates, the Clinical Congress, the Council, and committees of the Society.

VIII. SCIENTIFIC ASSEMBLY

Purpose: To remove the provision that the Council arrange the scientific assembly. This function is now carried out by the Committee on Program of the Scientific Assembly.

Amendment

ARTICLE VIII—Scientific Assembly

Section 2—Meetings

Par. 1. General. (Delete the underlined words and add words in capitals)

General meetings of the Scientific Assembly OF THE SOCIETY shall be held annually, General meetings of the Scientific Assembly shall be arranged by the Council which shall select the persons to preside. AT A TIME AND PLACE DESIGNATED BY THE COUNCIL. THE ANNUAL MEETING OF THE HOUSE OF DELEGATES SHALL BE HELD DURING THE WEEK OF THE SCIENTIFIC ASSEMBLY.

IX. ORGANIZATION AND OPERATION OF BOARDS AND STANDING COMMITTEES

Purpose: To facilitate the preparation of the budget of the Society.

Amendment

ARTICLE XI—Divisional Boards and Committees

Section 4—Organization and Operation of Boards and Standing Committees (Delete the underlined words)

Each divisional standing committee shall submit to its divisional board for transmittal to the Council a budget for the fiscal year.

Per Directive of House of Delegates
December 11, 1969

X. CHANGE IN DIVISIONAL BOARDS

Purpose: To combine the present Legislation and Public Relations Divisions in a new Public Affairs Division under which the following committees would be included:

Committee on State Legislation
Committee on National Legislation
Committee on Public Relations
Committee on Public Affairs (New)

Amendment

ARTICLE XI—Divisional Boards and Committees

Section 1—Divisions (Delete the following divisions)

Legislation Division
Public Relations Division
(Add the following Division)
Public Affairs Division

Section 3—Divisional Standing Committees (Delete the following paragraphs in their entirety)

Paragraph (B) Legislation Division
Paragraph (E) Public Relations Division
(Add the following Paragraph)
Public Affairs Division
  Committee on State Legislation
  Committee on National Legislation
  Committee on Public Relations
  Committee on Public Affairs
(Reletter paragraphs as necessary)

Section 5—Duties of Standing Committees (Add the following new numbered paragraph)

Committee on Public Affairs. The Council shall annually nominate to the House of Delegates a Committee on Public Affairs to consist of not less than eight members and shall nominate the chairman thereof. The function of this committee shall be, in consultation and cooperation with the Committee on State Legislation, the Committee on National Legislation, and the Committee on Public Relations, to plan a program of political education for members of The Society, such program to be conducted on a year-round basis and to be implemented by the office of the Executive Director. The Committee shall also maintain liaison with the Board of Directors of the Connecticut Medical Political Action Committee (COMPAC) and shall encourage support of COMPAC among the members of The Society.

SUMMARY OF ACTIONS COUNCIL MEETING

Thursday, February 19, 1970

I. Attendance

Present in addition to the Chairman, Dr. S. J. Martin, and the Vice-Chairman, Dr. K. F. Brandon, were: Drs. Granoff, Weber, Jr., Edson, Grendon, Abbot, Dean, Polivy, Rogol, Cramer, Harwood, Petrie, Roch, Grant, Nemoitin, Friedberg, McDonald, Pelz, and Root, Jr.

Also present were: Mrs. Lindquist, Dr. Patterson (Dean, UConn). Dr. Redlich (Dean, Yale), Commissioner Foote (State Health Department), Mr. Donelan (AMA), Mr. Gordon (Executive Director, HCMA), Mr. Olson (Executive Secretary, FCMA) and Dr. Richards.

Absent were: Drs. Gardner, Fabro, Gallo, Wilson, Jr., Purnell, Johnson, Gorin, von Glahn, Palomba and Klare.

II. Routine Business

Approval of Minutes

As printed and distributed, it was VOTED to approve the minutes of the meeting of January 21, 1970.

Life Memberships

It was VOTED to approve applications for Life Membership received from the following eligible Active Members:

Mary M. Allen, West Hartford (HCMA)—1970
Nicholas E. Creaturo, Bridgeport (FCMA)—1970
Wendell C. Hall, West Hartford (HCMA)—1971
Morris A. Hankin, New Haven (NHCMA)—1970
Moses D. Lischner, Hartford (HCMA)—1970
John S. Papa, Fort Lauderdale, Fla. (NHCMA)—1970
Albert Rubin, West Hartford (HCMA)—1970
William F. Storms, Wethersfield (HCMA)—1970
Edward E. Williams, Naugatuck (NHCMA)—1970

CSMS Dues Exemptions

It was VOTED to exempt from payment of CSMS dues the following Active Members for the reasons and periods stipulated:

Anthony P. Cipriano, Hamden (NHCMA)—1970—Postgraduate Education.

Donald Fishman, Orange (NHCMA)—1970—Physical Disability.

Roger A. Graham, New York (NLCMA)—½ year 1969; full year 1970—Postgraduate Education.

Lloyd M. Wilcox, Jr., New Haven (NHCMA)—½ year 1969; full year 1970—Military Service.

Date of Next Meeting

The next Council meeting is scheduled for Wednesday, March 25, 1970.

III. Old, New and Special Business

Election of Student Members

It was VOTED to elect to Student Membership the following residents of Connecticut who are attending medical schools in the United States:

Paula L. E. Blake, Box 9, 55 Elizabeth Street, Hartford
University of Connecticut—1973
Pre-Med: St. Joseph's College
Parent: William G. Blake

Richard A. Rasche, 69 Bonny View Road, West Hartford
University of Connecticut—1973
Pre-Med: University of Michigan
Parent: Harold A. Rasche

Michael J. Raybeck, 40 Westville Avenue, Danbury
Tulane University—1971
Pre-Med: St. Mary's of Maryland
Parent: Michael T. Raybeck

Robert D. Russo, Jr., 208 Brooklawn Avenue, Bridgeport
Tulane University—1973
Pre-Med: Fordham University
Parent: Robert D. Russo, M.D.

Reports—Fiscal Advisory Committee

It was VOTED to take the following actions on a series of recommendations presented by the Fiscal Advisory Committee:

(a) *AMA Automotive Seminar, Boston, Massachusetts, May, 1970:* To authorize Harry P. Engel, Bridgeport, a member of the CSMS Committee on Accident Prevention, to attend this Seminar as a representative of the Society, and to reimburse him for usual expenses incurred therby in an amount of up to $50.

(b) *Membership Dues, Council of New England State Medical Societies:* To table consideration on this item pending receipt of a report from the CSMS Delegates to CNESMS on the question of continuing membership in that organibation.

(c) *AMA Rural Health Conference, Milwaukee, Wisconsin, April 9-10, 1970:* To authorize a member of the CSMS Committee on Rural Health, William H. Pomeroy, Poquonock, to attend this Conference as a representative of the Society and to reimburse him for usual expenses incurred thereby in an amount up to $225.

(d) *Purchase of Office Equipment:* To authorize the staff to purchase a new floor cleaning and polishing machine to be used for building maintenance, at an approximate cost of $400.

(e) *Membership, Connecticut Chamber of Commerce:* To authorize enrolling the Society as a member of the Connecticut Chamber of Commerce, for a one-year trial period, and to pay membership dues to the CCC in an amount not to exceed $100.

(f) *AMA Regional Conference on Medical Quackery-Chiropractic, Boston, Mass., 5/1/70:* to authorize the Chairman of the Committee on State Legislation, Isadore H. Friedberg, or a member of that Committee designated by him, to attend this Conference as a representative of the Society, and to reimburse the representative for usual expenses incurred thereby in the amount of up to $50.

(g) *Connecticut Physicians' Art Association:* To make available to the president of the CPAA an amount of up to $200, to be drawn on by him as needed to defray the costs of holding an art exhibit in conjunction with the Society's Annual Meeting in May, 1970.

(h) *4th National Congress on Socio-Economics of Health Care, Chicago, Ill., 3/20-21/70:* To authorize one representative of the Society, to be designated by the Chairman of the Committee on Third Party Payments from among the members of the Committee, to attend this Congress, and to be reimbursed for usual expenses incurred thereby in the amount of up to $250.

Report—Committee on Preliminary Study of Nominations

Acting on the report of this Committee, and having made a number of amendments thereto, the Council VOTED to approve the report, as amended, and to transmit the amended report to the House of Delegates in May, 1970, as the Nominating Committee's recommended slate of nominees for election by the House.

The slate of CSMS officer nominees follows:

President—Morris A. Granoff, New Haven (without election)

President-Elect—Frederick C. Weber, Jr., Greenwich

Vice-President—David A. Grendon, Sharon

Secretary—Reginald C. Edson, Hartford

Treasurer—Bernard A. Burnham, Waterbury

Speaker of the House—Kenneth F. Brandon, Hartford

Vice-Speaker of the House—Frank K. Abbot, Waterbury

AMA Delegates—J. Alfred Fabro, Torrington and Michael A. Dean, Bridgeport

Alternate AMA Delegates—E. Tremain Bradley, Norwalk and Sidney L. Cramer, Hartford

Councilor-at-Large—Stevens J. Martin, Hartford

Pursuant to this action, a series of recommendations relating to nominations were approved as follows:

(a) *Advisory Committee to State Board of Examiners for Nursing:* It was VOTED to delete this Committee, after 1970, and to request the staff to draft a suitable amendment to the By-laws to accomplish this purpose for introduction at the May meeting of the House of Delegates. When the amendment has been adopted, the State Board will be notified than an ad hoc committee will be furnished as needed.

(b) *Cancer Coordinating Committee:* It was VOTED to respond to a suggestion of the Committee chairman, Wayne P. Whitcomb, by requesting the Committee to study the validity of the Committee, in terms of current thinking, and to make recommendations to the Council concerning its possible restructuring in terms of composition, functions, objectives, etc.

(c) *Advisory Committee to Cerebral Palsy Association:* It was VOTED to delete this Council-elected Committee and to inform the Cerebral Palsy Association that, when needed, ad hoc advisors will be furnished.

(d) *Conference Committee with State Dental Association:* It was VOTED to delete this Council-elected Committee and to notify the State Dental Association that, if and when needed, qualified ad hoc CSMS conferees will be furnished.

(e) *Delegates to State Medical Societies:* It was VOTED to change the present policy that all Delegates to State Medical Societies must be members of the Council or have been members of the Council within four years of their election, to a new policy that requires that *only one* of each pair of such Delegates meet these qualifications. It was further VOTED that, concerning the Medical Society of the State of New York, the President shall be the Delegate and the President-Elect shall be his Alternate Delegate in the event that the President is unable to serve.

Report—Liaison Committee with the Welfare Department

It was VOTED to receive as information, and with thanks, a report of the Committee submitted by its chairman, Charles Polivy, on the proceedings of a meeting of the Committee with the State's Professional Policy Committee, February 5, 1970. In brief, the report stated that further discussion was held on the CSMS-advocated revisions of the present Medicaid payment schedule and that a final decision of the Professional Policy Committee thereon was being awaited.

Recommendations—Committee on Public Health

(a) *Statement on Health Education in Schools:* It was VOTED to approve, in principle a statement submitted by the Committee (Advisory Committee on School Health) as follows:

   (1) That the Council reaffirm the importance of the Connecticut State Medical Society's endorsing and supporting effective health education legislation.

   (2) That the Society endorse plans for disseminating information as widely as possible concerning what health education really is and why there is a need for it.

(b) *Resolution re P.A. 360 re Ear Piercing:* It was VOTED to receive as information a resolution on P.A. 360, a 1969 act of the General Assembly which prohibits ear piercing by any person other than a person licensed to practice medicine and surgery in Connecticut. Noting that the new statute, in full, had been published in the November, 1969 issue of *CSMS Newsletter*, the Council further VOTED to bring the matter to the attention of the Connecticut Nurses' Association and the Connecticut League for Nursing.

(c) *Resolution re Air Pollution:* It was VOTED to approve, in principle, a resolution on this subject, submitted by the Committee, and to apprise the Commissioner of Health, Dr. Franklin M. Foote, of this action. The resolution follows:

WHEREAS: Air pollution has always been a serious concern of physicians. Some pollutants are known to have a direct acute adverse effect upon health; others have been suspected of contributing to the cause of certain diseases after prolonged exposure at relatively low concentrations. There is little question about the ill effects of oxides of sulfur on health when inhaled both in pure form and particularly in combination with other air pollutants; and

WHEREAS: With population growth continuing at a rapid pace, resulting in an ever increasing demand for services and products which require the combustion of greater amounts of fossil fuels for their production, the quality of the air we breathe will, without doubt, continue to deteriorate, unless firm steps are taken to control the level of products of combustion in the atmosphere; therefore be it

RESOLVED: That the Council of the Connecticut State Medical Society support, in principle, the efforts of the Connecticut Clean Air Commission to reduce the concentration of oxides of sulfur in ambient air by limiting the sulfur content of fossil fuels used in combustion processes to 1% or less by weight.

Report—Committee on Third Party Payments

It was VOTED to accept a report filed by the Committee on Third Party Payments which consisted of a detailed analysis and evaluation of an insurance and/or prepayment plan proposal submitted by the Board of Directors of HCMA. One editorial change was made in the text; i.e., change the phrase "Relative Value Schedule" to read "Relative Value Scale" in Section (3)—Criteria for Foundation Endorsement. It was further VOTED to approve the report's three recommendations as follows:

(1) That the Council approve this report of the Committee on Third Party Payments and endorse its evaluation and conclusions with respect to the proposal of the HCMA Board of Directors.

(2) That a copy of the report be transmitted to the governing bodies of each of the component County Medical Associations for study and subsequent comment to the Council.

(3) That, since it is the Committee's understanding that the HCMA Board of Directors had earlier contemplated implementing its propos-

al as an independent function of that Association, the HCMA Board be urged by the Council to undertake a pilot HCMA membership survey on the foundation approach, as advocated under "Conclusions," and report the results of such survey to the Council.

Telephone Prescribing of Class A Narcotics

Through the medium of correspondence received from both state and Federal narcotics control agencies, President Martin again reminded the Council that Federal statutes and regulations take precedence over state statutes, that the telephone prescribing of Class A narcotics is still not legal in Connecticut, and that pharmacists are liable to be prosecuted if they fill such prescriptions on the telephone order of a physician. This ruling has already been publicized to the membership in the *CSMS Newsletter*. Dr. Martin's reminder was received as information.

Report—Committee on Public Affairs, Pro Tem

It was VOTED to accept as information a report filed by this Committee on matters considered at its organizational meeting on February 18, 1970. In brief, the report advocated that a political education program for members of the Society be planned and implemented forthwith, and stated the objectives of such program as follows:

(1) Education of all our members about the need for political legislative action.

(2) Provide political intelligence gathering machinery coordinated with information from the legislative committees and the public relations committees and to disburse it to our constituents.

(3) The political education activities should be year round and should involve both long-term and immediate objectives.

(4) The machinery of political education should work down through the county and local societies even to individual candidate support committees.

Progress Report—Committee on Medical Economics and Insurance

The Council was apprised that the Committee Chairman, M. David Deren, Bridgeport, is in the process of preparing a comprehensive report on the Committee's in-depth study of the problems associated with professional liability (malpractice) insurance. It is anticipated that such report will be ready for presentation to the Council by the latter part of March and that Dr. Deren will ask that the Council receive and discuss the report at a "special" meeting called for that purpose.

Communication—Commissioner of Health re Water Pollution

It was VOTED to receive as information, and with thanks, a combined written and oral presentation made by Commissioner Franklin M. Foote, State Health Department, concerning the water pollution hazards that arise when major highways have been, and are planned to be, constructed in close proximity to reservoirs. A reported case in point is the planned construction of "I-291 or similar highway in close proximity to the reservoir system of the Metropolitan District Commission (Hartford, Connecticut)."

The four main contributors to such polution from highways, either air borne or by drainage, are:

(1) Automobile emissions (lead, hydrocarbon compounds)

(2) Brake linings and undercoating (asbestos fibers)

(3) Spillage of hazardous materials (toxic chemicals) on the highways

(4) De-icing chemical compounds (converted to aerosols)

It was further VOTED to request the Executive Director to draft a subject resolution pointing out the hazards listed above, and to send a copy thereof to Commissioner Foote, Transportation Commissioner Conkling and to Governor Dempsey.

N.B.: *The foregoing is a summary of the proceedings and actions of the Council on January 21, 1970. Detailed minutes of the meeting are on file at 160 St. Ronan St., New Haven, for perusal by any interested member of the Society.*

The Connecticut State Medical Society offers placement assistance through the Physicians Placement Service, 160 St. Ronan Street, New Haven, Connecticut, 06511. This service is for the use of physicians seeking locations, as well as physicians seeking associates, and is without charge.

Placement Opportunities

PHYSICIAN who will be willing to work on a salary basis for one or two years with an opportunity for subsequent full partnership after approximately three additional years. Practice consists of general-medical pediatric type practice with the exclusion of obstetrics and major surgery.

GENERALIST OR INTERNIST—Growing central Connecticut residential community, fine schools, quiet country living. Twelve miles from 400 bed general hospital. For further information write or call William B. Lyons, M.D., R.D. #2, Kettletown Road, Southbury, Conn. 06488, Tele. 264-8884.

PEDIATRICS—Board certified or eligible wanted for association with Board man in a Connecticut shoreline community of 50,000. Close proximity to Yale Medical Center. Salaried first year, then partnership.

CAMP PHYSICIAN—for approximately 300 summer campers (boys and girls) at Winchester Center, Connecticut. 8 weeks period, beginning late June, 1970; would accept two physicians for consecutive four-week periods. Two R.N.'s in resident attendance. Salary open. Requirements: Must have Connecticut License; may be intern, resident, in practice or retired; with or without family.

MEDICAL DIRECTOR—40 hour week! All holidays! Regular vacations! No nights! All staff and equipment paid for by company. In short a high level professional staff position for a General Practitioner or Internist with a leading industrial firm in North Central Connecticut. Industrial experience not required but even part time exposure would be a plus. Will deal with various industrial health and safety problems and supervise a staff of five. Solid, well run firm. Excellent benefit program. Fine opportunity to grow. Starting salary $25,000. Naturally, all fees are paid by the client company. For completely confidential interview send curriculum vitae or call UNI/SEARCH, 15 Lewis Street, Hartford, Connecticut; 278-8040.

STUDENT HEALTH—Two immediate openings, University of Connecticut; competitive salary; campus of 14,000 in ideal rural setting; excellent fringe benefits and retirement; new wing being completed; access to all New England sports. Apply: Edward P. Wanderse, M.D., Acting Director, Health Service, University of Connecticut, Storrs, Connecticut 06268.

HILLSIDE HOME AND PRACTICE—Yalesville, Ct., midway between New Haven and Hartford. Location of 13 room, 3 story original farmhouse cannot be duplicated. Adequate space for office in home with 2-car garage, private garden area and panoramic view 15 miles to the East. Physician needed in this growing community between Wallingford and Meriden. Price $50,000 includes office equipment. For further information contact William W. Dickinson, M.D., 63 Hill Avenue, Yalesville, Connecticut 06492.

PEDIATRICIAN needed for multispecialty group in central Connecticut. Excellent starting salary; bonus arrangement, partnership after two years. Contact R. Postl, Business, Manager, Grove Hill Clinic, New Britain, 203-225-8471.

VACANCY FOR A PART-TIME PHYSICIAN—to serve as District Medical Consultant in Hartford. Duties involve essentially reviewing medical report, ascertaining disabilities, and advising vocational counselors in related medical matters. Connecticut license required. 4 hours per week. Job would be particularly interesting to physicians who are phasing out current private practice. For further information, please contact Mr. Edward C. Swift, District Supervisor, Connecticut State Division of Vocational Rehabilitation, Hartford District Office, 122 Washington Street, Hartford. Telephone 566-4103.

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ANYONE INTERESTED IN THE ABOVE IS ASKED TO CONTACT THE EXECUTIVE DIRECTOR'S OFFICE, 160 ST. RONAN STREET, NEW HAVEN, CONNECTICUT 06511.

Placement Wanted

INTERNAL MEDICINE—GASTROENTEROLOGY—33 years of age wishes group or associate type practice in Connecticut. Will consider partnership in the Fairfield area. Eligible with National Boards. Military obligation completed.

SURGERY—32 years of age wishes solo or associate type practice in Connecticut. Military obligation completed. Eligible with National Boards. Presently in practice.

OBS & GYN—33 years of age wishes solo, group or associate type practice in Connecticut. With Connecticut license.

ANESTHESIOLOGY—34 years of age wishes solo type practice in Connecticut. Certified with National Boards. Presently in practice. Interested in directing a department of Anesthesiology. Available immediately.

EMERGENCY ROOM—39 years of age wishes to practice in Connecticut. Passed National Boards. Military obligation completed in July 1970. Connecticut license.

SURGERY—36 years of age wishes group or associate type practice in Connecticut. Military obligation completed. Certified with National Boards. Presently in practice.

UROLOGY—37 years of age wishes institutional type practice in Connecticut. Interested in a full time academic post. Eligible. Presently in practice. Available immediately.

GENERAL PRACTITIONER — 32 years of age wishes emergency room position in Connecticut. Presently in practice. Military obligations completed. Connecticut license in process.

PATHOLOGIST—39 years of age with Connecticut license seeking directorship of laboratory of similar position. Has eight years experience as laboratory director. Available when right position arises.

UROLOGIST—31 years of age with National Boards wishes group or associate type practice in Connecticut. Military obligation completed.

PHYSICIAN—43 years of age interested in emergency room or as a house physician in the Fairfield area. Eligible with National Boards. Available immediately.

INTERNIST—30 years of age with National Boards wishes associate type practice in Connecticut. Military obligation completed.

OB & GYN—30 years of age. Eligible with National Boards wishes group or associate type practice in Connecticut. Available in July when military obligation completed.

INTERNIST—35 years of age wishes group or associate type practice in Connecticut. Eligible with National Boards. Presently in practice as chief of medicine. Available in July when military obligation completed.

UROLOGIST—31 years of age wishes group or associate type practice in Connecticut. Eligible. Military obligation completed.

DERMATOLOGIST—30 years of age wishes solo, group or associate type practice in the Fairfield County area. Certified with National Boards. Presently in practice. Available when military obligation completed in July.

GENERAL SURGERY—33 years of age wishes group or associate type practice in Connecticut. Certified with National Boards. Available when military obligation completed in July.

INTERNIST—31 years of age wishes to practice in Connecticut. Available upon request.

RADIOLOGIST—34 years of age wishes group or associate type practice in Connecticut. Eligible with National Boards. Military obligation completed.

OPHTHALMOLOGIST—31 years of age wishes group or associate type practice in Connecticut. Eligible with National Boards. Presently in practice. Available when military obligation completed in July.

DERMATOLOGIST—35 years of age wishes group type practice in Connecticut. Presently in practice. Certified. Available in July.

ORTHOPEDICS—31 years of age wishes group or associate type practice in Connecticut. Eligible. Available in July.

RADIOLOGIST—31 years of age wishes group or associate type practice in Connecticut. Eligible with National Boards. Available when military obligation completed in June.

INTERNIST—31 years of age wishes group or associate type practice in Connecticut. Eligible with National Boards. While serving in the Air Force he held positions as Chief of Medicine and Chief of Hospitals. Presently in practice. Available when military obligation completed in July.

MEDICAL DIRECTOR—54 years of age wishes institutional type practice in Connecticut. Eligible. Presently in practice. Connecticut license.

NEUROLOGIST—30 years of age, Eligible with National Boards wishes group or associate type practice in Connecticut. Would prefer practice in a multispecialty group preferable with another neurologist.

INTERNIST—30 years of age, Eligible with National Boards wishes solo, group or associate type practice in the south west part of Connecticut. Would consider part or full time hospital practice with some subspecialty work in renal or dialysis medicine. Military obligation will be completed in July, available then.

UROLOGIST—52 years of age, Certified, wishes solo or group type practice in Connecticut. Available immediately.

PATHOLOGIST—34 years of age, Certified with National Boards, wishes associate type practice in Connecticut. Presently in practice.

OB & GYN—32 years of age, Eligible, wishes solo, group or associate type practice in Connecticut. Presently in practice, with Connecticut license.

UROLOGIST—32 years of age, with National, Boards, wishes group or associate type practice in Connecticut. Would prefer to go in with at least one other man fairly near a good size hospital. Presently in practice.

PSYCHIATRIST—38 years of age, Eligible with National Boards wishes to practice in Connecticut. Presently in practice. Has done a good deal of inpatient and out-patient work.

INTERNIST-ALLERGY—31 years of age, Certified, with National Boards, wishes group or associate type practice in Connecticut. Presently in practice with Connecticut license. Military obligation completed.

PREVENTIVE MEDICINE—35 years of age, wishes institutional or industrial type practice in Connecticut. Presently in practice with Connecticut license. Available immediately.

INTERNIST—32 years of age, Eligible with National Boards, wishes solo type practice in Connecticut. Presently in practice with Connecticut license.

ANESTHESIOLOGY—38 years of age, Certified, wishes group or associate type practice in Connecticut. Presently in practice with Connecticut license. Military obligation completed. Available immediately.

SURGEON—35 years of age, Certified, wishes group, associate or institutional type practice in Connecticut. Presently in practice with Connecticut license. Military obligation completed. Available immediately.

PEDIATRICS—31 years of age, Eligible with National Boards, wishes group type practice in Connecticut. Group practice at large teaching hospital or university hospital preferred.

GENERAL PRACTICE OR PEDIATRICS—32 years of age wishes part-time position for the month of July.

ANYONE INTERESTED IN THE ABOVE IS ASKED TO CONTACT THE PHYSICIANS PLACEMENT SERVICE, 160 ST. RONAN STREET, NEW HAVEN, CONNECTICUT 06511.

Drug Interaction Symposium
May 6, 1970

The Hotel Sonesta in Hartford will be the scene of a *Drug Interaction Symposium* for Connecticut physicians and pharmacists on Wednesday, May 6, 1970. A distinguished panel of experts representing the physician, hospital administrator, and pharmacist will convene to discuss various aspects of the drug interaction problem.

The program, sponsored by the University of Connecticut School of Pharmacy in cooperation with the Connecticut Pharmaceutical Association and the Connecticut Society of Hospital Pharmacists, is made possible through the courtesy of Lederle Laboratories.

Connecticut physicians and pharmacists will be contacted by mail. They are requested to complete the self-addressed postcard which is enclosed in the mailing so that proper arrangements may be made for the registrants. We urge all Connecticut physicians to attend this important symposium. Because of the complexity and increased potency of today's drugs it is more important than ever for pharmacists and physicians to be kept up-to-date with the latest and best information on drug interaction possibilities.

Where?

Plaza Room, Hotel Sonesta (Formerly Hotel America), Hartford.

Time?

2:00 p.m. to 4:30 p.m.

The Panel?

Dale G. Friend, M.D., Associate Clinical Professor of Medicine, Harvard Medical School; Irving Rubin, R.Ph., Editor and publication Director, *Pharmacy Times;* William E. Hassan, Jr., Ph.D., Director, Peter Bent Brigham Hospital, Boston, Mass.; Moderator: Gale L. Smith, Manager of Customer Relations, Lederle Laboratories, Pearl River, N.Y.

A question and answer period will follow.

Then What?

Reception—4:30 p.m. to 6:00 p.m.

More?

Wives most welcome.

And?

No fee of any type required for attendance.

NEW...

SUSTAINED-RELEASE VITAMIN C

CEVI-BID

500 mg. capsules maintain optimal levels around-the-clock on b.i.d. dosage

When Vitamin C is taken in ordinary tablet form, the rise in blood levels is rapid, but Vitamin C is as rapidly excreted and blood levels drop accordingly.

In CEVI-BID, medication is released at a smooth, continuous, predictable rate dependent only upon the presence of fluid in the G.I. tract and independent of pH or other variables.

CEVI-BID maintains optimal blood levels of Vitamin C, and avoids "peak and valley" effects of ordinary Vitamin C tablets.

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AROUND THE STATE

New Haven County

Board of Governors Meeting
New Haven County Medical Association

March 5, 1970

The Board of Governors of The New Haven County Medical Association met on Thursday, March 5, 1970 at The Colonial House in Hamden, Kurt Pelz, M.D. presiding. Attendance was 28 out of a possible 35.

After nearly a year of recent meticulous study under the Chairmanship of Louis Cappucci, M.D. and ten years of intermittent study, the Board of Governors accepted Dr. Cappucci's Public Relations Committee report and voted to engage the services, on an annual basis, of a full time professional public relations firm. The firm named was Lee Eisenberg Associates of Hartford, who already are advisors in public relations to The Connecticut Chapter of the American Academy of General Practice and the Waterbury Medical Association.

In commenting on the entrance of a paid professional public relations firm into the activities of the Association, President Kurt Pelz pointed out that it coincided quite opportunely with the very recent extensive efforts of the A.M.A. to focus attention on the local component County's roles in the everyday public relations and community service aspects of medical care delivery.

It is hoped that the public relations firm, in addition to developing a local New Haven County program, will be able to coordinate the county efforts into the ongoing A.M.A. and Connecticut State Medical Society programs in a highly effective manner.

New Haven County's veteran councilor, Stewart J. Petrie, M.D. reported on 11 items of recent Connecticut State Medical Society council business. The council activities are reported elsewhere in Connecticut Medicine.

Dr. John J. Mendillo reported that the New Haven County Medical Associations' Woman's Auxiliary is doing a fine job, but is handicapped by a rather minimal membership. The Board of Governors instituted measures that are designed to begin a program of closer ties with and greater encouragement to the Auxiliary.

Dr. James H. Root, Jr. in speaking of COMPAC stated "Things have gone from chaos to pathos, but there is a brighter light on the horizon." As long time supporters of COMPAC, in spirit if not in numbers, the New Haven County Medical Association has been indeed chagrined to find the extremely important matter of political action to support legislative goals sink into its present condition of disarray on the State-wide scene. The Board evidenced its continuing support for the COMPAC principle, having appreciated the successful pioneering efforts of organized labor with their COPE political action arms which today are probably the single most effective political action organizations in the country.

A considerable amount of time was spent in introducing two important newer concepts concerning the delivery of medical care services. They are:

1. The Himler Report of the A.M.A.
2. The Hartford County Medical Association's "Foundation" plan.

Both concepts are now in the process of receiving a thorough evaluation by the Board and its appropriate committees.

Like doctors all over the United States, the members of the Board of Governors reflected their concern over the nation-wide trend of pre-occupation with matters legal.

Reflecting their joint concern over the difficulties that the legal process seems to be engendering throughout the country; the members of the Board of Governors focused their attention on the specific matter of medical malpractice. The following resolution concerning the nation-wide crisis in malpractice was directed to the attention of the Council of the Connecticut State Medical Society; "The New Haven County Medical Association requests that the Judicial Committee and the Council proceed with all deliberate speed to resolve the Malpractice Crisis."

After the strenuous activities of the meeting and for the first time in the 1969-1970 season, the social hour and dinner that followed were not occupied with any further business.

Respectfully submitted,
William L. West, M.D., *Clerk*

Medical Grand Rounds
Yale-New Haven Hospital
Chronic Renal Failure Treated by Transplantation

Frederick Lee Sachs, M.D. and Lewis Landsberg, M.D., Editors
Pamela Brooten, Assistant Editor

The patient is a 31 year old Negro male who was admitted to Yale-New Haven Hospital for the first time on January 17, 1969 because of renal failure. Hypertension was first detected in 1964 but the patient did not seek medical attention until January of 1969 when he presented at the St. Joseph's Hospital in Bridgeport complaining of weakness and decreasing urinary output. On that admission his BUN was 180 mg. % and creatinine 24 mg. %. After a single peritoneal dialysis he was transferred to Yale-New Haven Hospital for further care.

On arrival at Yale, his blood pressure was 150/110 and he was in marked congestive heart failure with a pericardial friction rub. His urine output was less than 100 cc. per day. Laboratory data included a BUN of 192 mg. %. and a creatinine of 21.4 mg. %. Retrograde pyelography demonstrated small kidneys without evidence of obstruction. He was treated with Apresoline and digitalis and was placed on a restricted protein diet. Peritoneal dialysis was begun on a weekly basis.

Soon after commencing biweekly dialysis, it became apparent that the chronic dialysis program was not meeting the patient's physical or psychological needs. He was unable to work because of the requirement of biweekly dialysis and became increasingly depressed. His family recognized the deterioration in his mental outlook and a sister volunteered to donate a kidney in the hope that a successful transplant would improve the patient's outlook. She was admitted to the Yale-New Haven Hospital where her renal function was thoroughly evaluated and found to be normal. In addition, she was seen by the psychiatrist associated with the transplant team. He examined the patient with regard to her reasons for offering a kidney and assessed her psychological strengths and weaknesses. She was found to be an acceptable donor in all respects. Tissue typing was performed and revealed that there was an excellent match, which raised the chance of achieving a successful transplant. On March 27, 1969, the patient received a transplant from his sister. His urinary output immediately following transplantation was good and 3 hours after surgery he had put out 550 cc. of urine.

Since transplantation the patient has had at least 3 episodes of rejection characterized by fever, decreased urine volume, reduced creatinine clearance and tenderness over the transplant site. Each episode has been treated successfully with large doses of steroids, increase in anti-hypertensive medication, and reduction in salt intake. He is maintained on Imuran and prednisone and has a daily urine volume of 1800 cc. His urine osmolarity is between 525 to 675 milliosmoles and his BUN is around 10 mg. % with a creatinine of 1.1 mg. %.

The patient's present admission was prompted by fever and abdominal pain. Evaluation revealed evidence of pancreatatitis with an amylase of 826 units and a lipase of 6.6 units. His abdominal distress responded to Nasogastric suction but has recurred at frequent intervals. On June 26th he underwent exploratory laporatomy at which time a fist-sized mass of necrotic pancreas was discovered. Post-operatively he has continued to have episodic abdominal pain and amylase elevations consistent with chronic pancreatitis. Throughout his present hospitalization his renal function has remained excellent.

DR. LEWIS LANDSBERG: Thank you, Dr. Meehan. Are there any questions?

DR. PHILIP K. BONDY: Was there any relationship between the attacks of abdominal pain and the level of steroids used?

DR. JOHN MEEHAN: No association was noted.

DR. HOWARD SPIRO: How did the attacks of pancreatitis originally manifest themselves? Did he

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DR. FREDERICK LEE SACHS, Instructor in Medicine, Yale University School of Medicine, New Haven, Conn.

DR. LEWIS LANDSBERG, Chief Resident in Medicine, Yale-New Haven Hospital, New Haven, Conn.

have pain, elevated amylase, and impressive physical findings, or merely pain and enzyme changes?

DR. MEEHAN: His attacks were characterized by pain, fever, and abdominal tenderness.

DR. JOHN FORREST: Was the patient given a choice between chronic dialysis and transplantation?

DR. FRANKLIN H. EPSTEIN: Yes. He was most anxious to undergo transplantation.

DR. LANDBERG: Dr. Michael Kashgarian will discuss the pertinent pathology.

DR. KASHGARIAN: In every kidney we have studied following transplantation there has been some morphological evidence of rejection. The problem for the pathologist is to determine the severity and acuteness of the rejection. Rejection reactions fall into three distinct clinical and anatomical entities. The first is the hyperacute reaction which literally takes place in front of the surgeon's eyes as he transplants the kidney. This reaction is probably related to the action of pre-formed humoral antibody. In another type of hyperacute reaction, one sees a Schwartzman-like phenomenon related to the presence of endotoxin within the donor kidney. The Schwartzman reaction has been associated with intravascular coagulation and cell necrosis.

The most common form of rejection takes place sometime after transplantation, usually within the first week, and almost every transplant patient experiences a reaction of this type during the first six months.

The morphology of primary acute rejection includes interstitial edema and infiltration. Small lymphocytes and lymphocytoid cells are seen in the region of vessels and perivascular areas. Polymorphonuclear leukocytes and eosinophils are seen as well. The small venules are filled with thrombotic material and there is occlusive thrombosis in the capillaries and small venules. The glomerulii are not involved to any significant degree. The mechanism of this reaction is probably primarily related to the presence of sensitized cells, but polymorphonuclear leukocytes, edema, necrosis, and thrombosis suggest that other forms of antigen-antibody reactions may be involved.

The most common type of rejection occurs because we are unable to totally eliminate the body's rejection mechanism and after the transplant has remained in the recipient's body for some time, evidence of chronic changes are seen. This rejection is also related to the development of humoral antibody and is manifest clinically by proteinuria. Histologically one sees membranous glomerulonephritis and intimal proliferation.

DR. LANDSBERG: Dr. Lytton will discuss the surgical aspects of renal transplantation.

DR. BERNARD LYTTON: I think it can now be said that the scientific dream of transplanting new organs into people who have destroyed their own has become a reality. This is not to say that we have solved the multitude of problems arising from immunological differences between people but we have now reached a stage where transplantation may be considered a therapeutic modality for patients with chronic renal disease. Apart from the immunological difficulties which shall be considered in detail in a few minutes, one of the most important problems concerns our need for donors. We have frequently met with some reluctance on the part of physicians caring for terminally ill patients to make organs available for transplantation. This stems from the fact that the patient's family is often under great stress during this period and the patient will derive no benefit from donating an organ after death. In addition, the physician becomes obligated to immerse himself in an unpleasant situation at the time of impending death which makes him less anxious to solicit permission for transplantation. At Yale-New Haven we have attempted to remove the responsibility from the physician by establishing a panel of physicians whose task it is to establish death in cases suitable for donation of organs.

At the present time the statistics from the Transplant Registry indicate that approximately one-half of transplants are performed from live, related donors and the other half come from unrelated donors; the bulk of the unrelated donors are cadaver donors. There is absolutely no advantage to transplantation from a living, non-related donor compared with a cadaver donor. If one investigates the possibilities of receiving a live donor kidney, it would appear that about 15% of patients with chronic renal disease would have available a suitable sibling or parent for transplantation. Thus it can be seen that to treat all patients with chronic renal failure by transplantation we will need to obtain 80% of our organs from cadaver donors. It is obvious that physicians must begin to think of transplantation when faced with a terminally ill patient who is a potential donor. We have found that our most common source has been from patients with brain hemorrhage, cerebral tumor, or from patients with severe head injuries. Other centers have successfully used donor kidneys from patients dying from major cardiac surgery.

The conditions which preclude someone as a donor are known renal disease, severe uncontrolled infection, hypertension, patients over 55, and, finally, patients with cancer other than those with brain tumor; the reason for this latter policy is that cerebral tumors do not metastasize whereas other cancers have been reported to have been transplanted with the kidney to the recipient.

Our surgical technique involves placement of the donor kidney in the right lower quadrant. The kidney is joined by means of its renal artery to the internal iliac artery of the host by an end-to-end anastomosis. If this is not possible, an end-to-side anastomosis to the external iliac artery is performed. The renal vein is anastomosed end-to-side to the external iliac vein. The ureter is implanted directly into the bladder. An alternative approach is to join the recipient's ureter to the donor kidney at the pelvis. We put a left kidney in the right lower quadrant for anatomical reasons so that the pelvis and ureter lies anteriorly and can be easily anastomosed. In addition, this technique brings the ureter close to the bladder and we have had no difficulty with ureteral blood supply in the patients to date. We have not been in the habit of removing the host's kidneys as a routine although bilateral nephrectomy is performed at some centers.

The donor's kidneys must be removed within an hour of death. This period before removal is referred to as the "warm ischemia" time. It is surgically possible to remove both kidneys in 15 minutes. The kidneys, once removed, are perfused with Ringer's lactate solution and heparin, first using a warm solution to wash out the blood and then a cold solution at –4° C. The kidneys can then be stored in the cold for up to 5 hours. This period of time in cold storage is referred to as the "cold ischemia" time. At the present time there are experimental units which enable one to store a kidney for up to 24 hours but this is currently more experimental than practical.

Dr. Kashgarian has previously discussed the pathology of rejection. Infection, of course, remains a difficult problem to control. From a technical point of view, our problems are primarily urinary in origin because we are unable to place tubes into these patients to allow for drainage prior to the healing of the anastomosis. With experience and meticulous technique, however, we have fortunately had few problems in this area.

The control of rejection primarily rests on the use of steroids in large dosages and anti-metabolites such as Imuran. We irradiate these patients with small doses directed to the transplant site although admittedly the evidence that this is effective therapy is meager. Thoracic duct fistula has been used extensively by the Boston group in an attempt to prolong graft survival but we have not been impressed with any marked improvement in graft survival. Antilymphocyte globulin has been used with variable success. Histocompatibility typing is employed at Yale and will be discussed by Dr. Kantor. The data obtained here and at other centers indicate that you have less late failures when there is good histocompatability, whereas if you have a bad match you get more failures; there have however been gross mismatches with good results and good matches with poor results. Van Rood showed that if there is less than on antigen difference, the one year survival was 73%; a two to three antigen difference dropped the survival to 60%; with a four antigen difference the survival dropped to 30%. Our data at Yale show that of six good matches, three had well functioning transplants, one had a moderate rejection, and two had severe rejections.

DR. LANDSBERG: Dr. Fred Kantor will discuss the problems of histocompatability.

DR. FRED KANTOR: The antigens involved in transplanatation immunology exert their effects by causing the host to produce an immune response which causes structural damage to the donated kidney, a phenomenon known as rejection.

The object of histocompatability typing is to try to detect antigenic differences between donor and recipient so as to reduce the chances of graft rejection.

The antigens involved in transplant rejection are ubiquitous. They are found on almost all cells in the body, but, unfortunately, are found in small amounts, if at all, on red blood cells. However, the circulating white blood cell provides us with an excellent source for the determination of histocompatability.

The idea is simple. We know that the best chance for graft success occurs where the donor and recipient are genetically identical. We, therefore, employ histocompatability typing in an attempt to find unrelated identical twins amongst the donor pool. Let us assume that a single locus on the chromosome was involved with histocompatability and that there were four alleles: A, B, C, and D. If two parents were heterozygotes at the major histocompatability locus, one parent might be AB and the other CD. There would thus be four possible combinations: AC, AD, BC, BD. If this couple had over four children, every fifth child might be expected to have an identical sibling with similar genotypes at the major histocompatability locus. There would therefore be a 20% chance of histocompatibility amongst siblings. Even if there were 50 or 100 alleles in the population, each family would still have only four alleles and each member woud have a 20% chance of having one sibling identical to himself in the histocompatibility sense. Unrelated individuals would vary a great deal.

In recent years, several workers have attempted to verify the theoretical assumptions mentioned above by observing known populations. Bach and Amos[1] studied a series of 29 families and compared data with several hundred unrelated donors. On a theoretical basis, if there was one locus with only one allele, all the related and unrelated matches would be good and you would get 100% matching. If you had two alleles on one locus, the percentage of good matches would be 80%. If we have only one locus, increasing the number of alleles leads to a fall in the percentage of good matches in both related and unrelated individuals. However, the fall in good matches is much more rapid in an unrelated population. Families are restricted in that the allele pool is small. The unrelated population is not restricted and, consequently, the number of good matches falls from 100% with one locus and one allele to 1% or 2% if there are 15 alleles, and soon down to no matches if there is an infinite number of alleles. If two loci are present, this reduces the restriction in the family and the number of good matches will fall precipitously, much like the unrelated population. The data of Bach and Amos indicate that about 30% of related pairs matched in their study contrasted with 1% of unrelated pairs. These data only fit with one locus and 15 or more alleles.

Histocompatibility tests may be done with sera in which we compare several sera with that of the patient and measure common antigens. Another test is called the mixed lymphocyte culture. It makes use of the ability of lymphocytes to undergo stimulation and division when exposed to a foreign major antigen. In this phenomenon, cells, when presented with a major histocompatibility antigen take up nucleic acid precursers as if they were going to divide. By labeling these precursers with radioactivity, one can tell if the cells are stimulated or not. The mixed lymphocyte culture enables us to measure differences between patient and donor. The disadvantage of this test is that it requires viable donor and recipient cells. We have an ample supply of recipient cells because these patients are in the dialysis program. However, the donor cells require us to have access to a patient before that patient becomes the donor. In cases of head injury or intracranial bleeding it is not often possible to perform this test because the cells take several days to become stimulated. We are hoping to develop techniques which will enable us to shorten this incubation time.

DR. LANDSBERG: Thank you Dr. Kantor. Dr. Brown will discuss some of the data from Yale-New Haven Hospital.

DR. ROBERT BROWN: The data of the last report of the Kidney Transplant Registry indicates that approximately 80% of live donor and 45% of cadaver donor transplants have a functional kidney at one year. Long term results show that almost 40% of cadaver kidneys survive for more than two years. The fact that small transplant centers are doing as well as the larger ones is encouraging.

At Yale-New Haven we have a small series, and meaningful analysis is difficult at this time. Two of the four live donor transplants are surviving at a mean of nine months. In our cadaver series we have transplanted 15 patients, in whom 5 kidneys or 33% are functioning at a mean duration of 12 months.

Our cases of transplant failure fit into two distinct categories. Five transplants were removed because of nonfunction. All five were lost because of rejection. Of these five, three patients have subsequently died. Seven patients died post-transplant of infection or infection-related causes.

These data might lead one to question why we should continue the transplantation program in view of this death rate. We consider the program acceptable for several reasons: 1) Because of our small number of transplants where a single result greatly influences our statistics, the success rates of live donor or cadaver donor transplants in our series do not differ significantly from those of the Kidney Transplant Registry. It is hoped that our results will improve with increased experience. 2) The alternative offered to patients with terminal renal failure is either peritoneal or hemodialysis which often leaves patients with undesirable symptoms and severely restricts diet and activities. All of our transplanted patients have elected to undergo transplantation rather than remain on chronic dialysis. 3) The surviving transplants are doing extremely well with the exception of the patient presented today, so that the quality of life in survivors is excellent.

The doses of prednisone and Imuran which we have been using can be so reduced that the steroid effects are minimal and certainly within the tolerable range. We have not had any major difficulties with Imuran tolerance.

I would like to direct my attention to the patient presented today and point out that he has had a 3 month bout of recurrent pancreatitis which has complicated a well-functioning living donor kidney transplant. The excellent function of this transplant has continued while prednisone has been eliminated. Imuran has been given in maintenance doses that keep his white blood cell count in the normal range.

The etiology of this prolonged pancreatitis is uncertain. We initially thought that it was secondary to steroids since these compounds have been implicated in pancreatitis in animal studies and in children. Pancreatitis has been previously observed in transplant patients on steroids. However, other etiologies must be considered, such as vascular-allergic pancreatitis, or possibly viral pancreatitis from cytomegalic inclusion virus. There was no evidence of biliary tract obstruction, hyperlipemia, or hyperparathyroidism.

ADDENDUM: With conservative management, the patient's pancreatitis resolved and renal function remained stable. He is now back at work and has made an excellent emotional recovery.

Reference

1. Bach, F. and Amos, D.: Hu-1: Major Histocompatability Locus in Man. Science. 165: 1506-1508, June 16, 1967.

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X-Ray of the Month

Section of Chest Diseases

Arnold B. Rilance, M.D.

R. C. #02-35-54, a 67 year old, white male, was admitted to the Yale-New Haven Hospital for evaluation of a massive infiltrate in the left upper lobe. He had a chronic cough for many years and was a heavy cigarette smoker. He was a known diabetic. For two months he had noted progressive swelling of his face, arms and legs, with decreased appetite and a 3 pound weight loss. He was quite weak.

On physical examination he was grossly dehydrated. B.P.—100/70; P.—110; Resp.—20; Temp.—100.2. There was a 3+ pitting edema of both forearms; 2+ edema of calves and ankles. Edema of the face and neck was noted. This was not relieved by diuretics and digitalis.

Chest examination demonstrated a flat percussion note over the left anterior chest with decreased breath sounds and bilateral rhonchi. A harsh systolic murmur was heard at the apex radiating to the left axilla. The liver was palpable 4 fingerbreadths below the costal margin. The spleen was not palpable. There was no abdominal ascites. Two 1.0 cm. nodes were palpable in the left axilla. The remainder of the physical examination was normal.

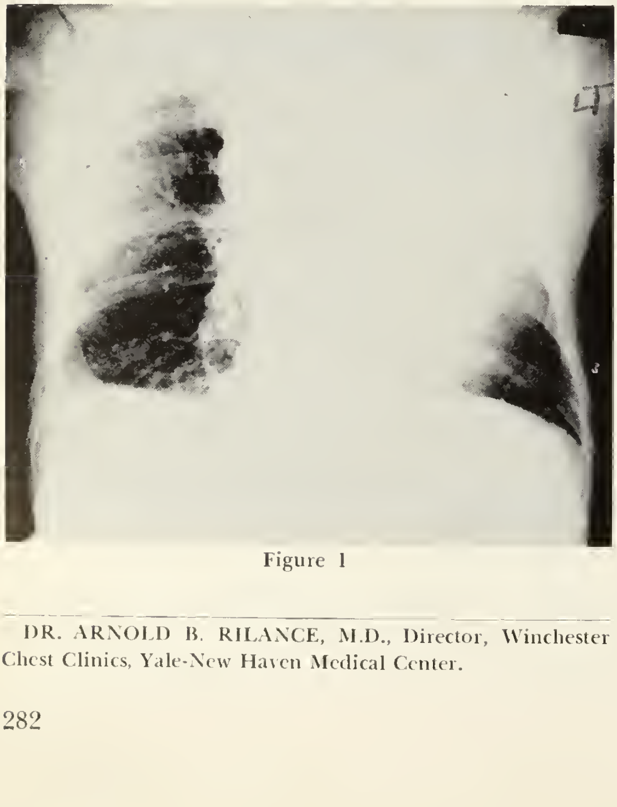


Figure 1

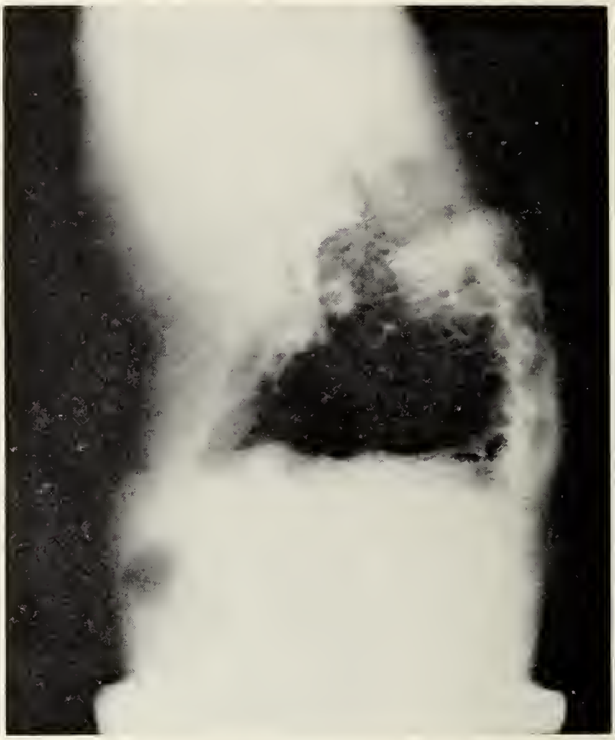


Figure 2

Figure 1 and 2

Conventional PA and lateral views of chest showing marked consolidation of left upper lobe. There is widening of the superior mediastinum to the right side.

Laboratory Tests:

CBC and urinalysis—normal. Electrolytes—normal.

Skin Tests:

PPD—negative. Fungus skin tests—negative.

Sputum:

Negative for AFB x 4

Cytology—positive x 3 for poorly differentiated carcinoma.

Peripheral Venous Pressure: (Antecubital)

3/31/69 — 360 mm. H_2O — before radiation

4/4/69 — 260 mm. H_2O — after minimal radiation to the mediastinum

---

DR. ARNOLD B. RILANCE, M.D., Director, Winchester Chest Clinics, Yale-New Haven Medical Center.

In view of the persistent edema of the face and upper extremities, the likelihood of a superior vena caval obstruction was seriously considered. A superior venacavagram was performed which showed complete obstruction of both subclavian veins.

Course of Illness:

Radiation therapy was started on 4/2/69 in an attempt to decompress the mediastinum. The V.P. dropped from 360 to 260 mm. H_2O after 4 days treatment. On 4/2/69, he had a seizure. A brain scan performed on 4/3/69 demonstrated increased uptake of radioactive material in both frontal regions. A diagnosis of cerebral metastases was made. On 4/11/69, he succumbed to his disease.

Final Diagnoses:

1. Poorly differentiated Ca. of left lung.
2. Mediastinal metastases. Superior vena caval obstruction.
3. Metastases to brain.
4. Diabetes mellitus.

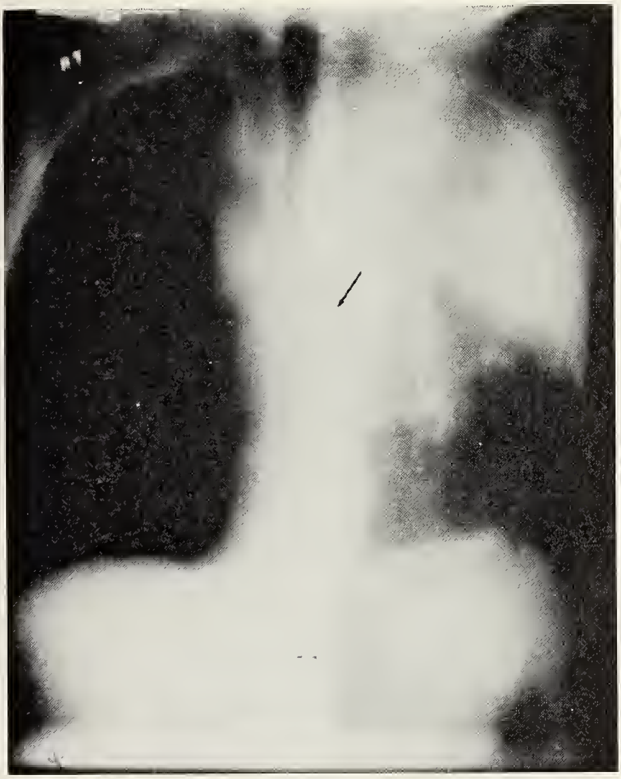


Figure 3

Laminagrams of mediastinum showing the faint outline of a narrowed left main bronchus, broadening at the main carina and bulging lymph nodes to the right of the trachea.

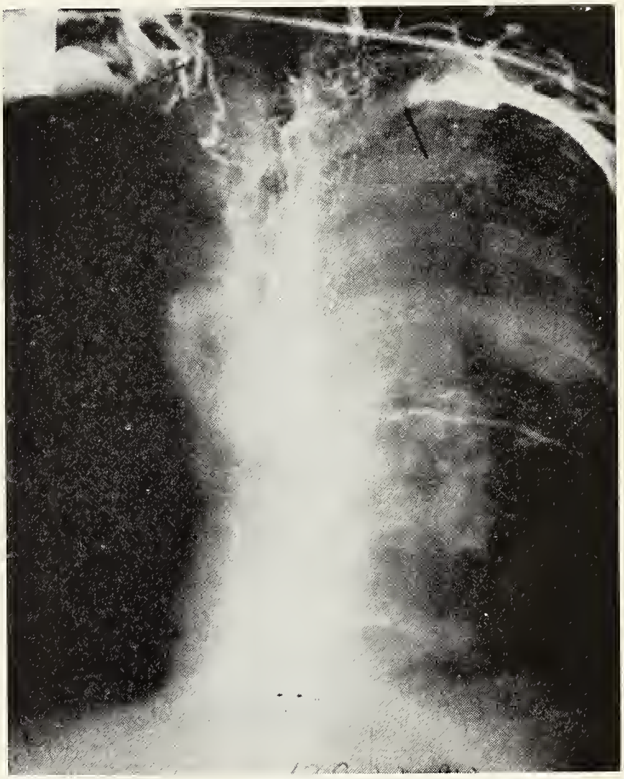


Figure 4

Superior venacavagram showing points of complete obstruction of both subclavian veins (arrows). Note outline of collateral venous circulation supporting venous return to the right side of the heart.

Electrocardiogram of the Month

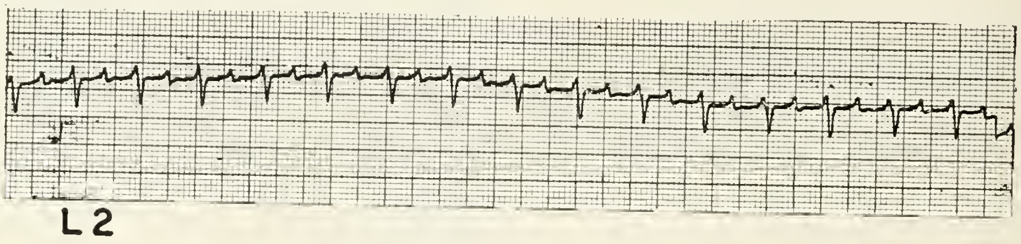
Montefiore Hospital and Medical Center
The Bronx, New York

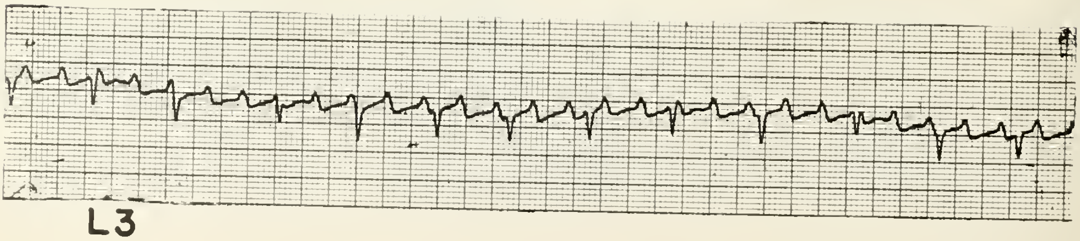
Editors
IRA L. RUBIN, M.D.
Head, Department of Electrocardiography
JULIAN FRIEDEN, M.D.
Associate Head, Department of Electrocardiography

Question 11. The rhythm is regular at a rate of 133 per minute. In lead II, between the QRS complexes, a sharp, narrow wave is seen. This wave is not a T wave because of its shape. Therefore, it must represent atrial activity. The diagnosis is either sinus or atrial tachycardia with a prolonged P-R interval, or possibly another P wave is superimposed on the QRS; the rhythm would then be atrial tachycardia or flutter with 2:1 block. The latter diagnosis is confirmed in lead III as the block varies from 2:1 to 3:1. The atrial rate can now be measured at 266 per minute. When the atrial rate exceeds 250, atrial flutter is usually present. Flutter can be further suspected from the absence of an isoelectric interval between the atrial beats. The final diagnosis is atrial flutter with varying block.

Question 12. The electrocardiogram shows a grossly irregular ventricular response. There are no visible P waves, but there are coarse f waves. The diagnosis is atrial fibrillation. Following left carotid sinus compression, there are bursts of slightly irregular, aberrantly conducted QRS complexes. These aberrantly conducted beats represent ventricular tachycadia. Supraventricular tachycardia with aberrant conduction cannot be ruled out. On the seventh beat in the lower strip the rhythm converts to a regular sinus rhythm.

The development of ventricular tachycardia is an unusual reaction to carotid sinus pressure during atrial fibrillation. Usually ventricular slowing occurs as vagal tone increases and conduction at the atrioventricular junction slows. The second unusual feature is the conversion of atrial fibrillation to normal sinus rhythm with carotid massage. Carotid sinus pressure may have serious side-effects. Standstill of the ventricles may occur. Other complications include hypotension and cerebrovascular accidents.





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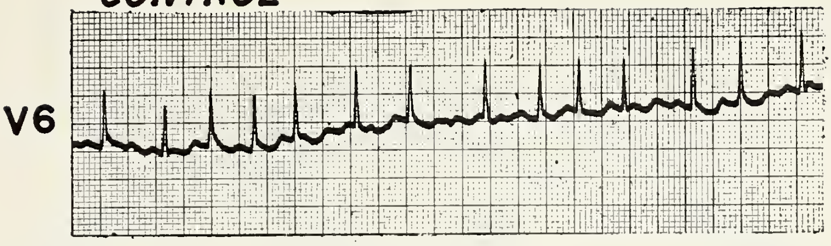
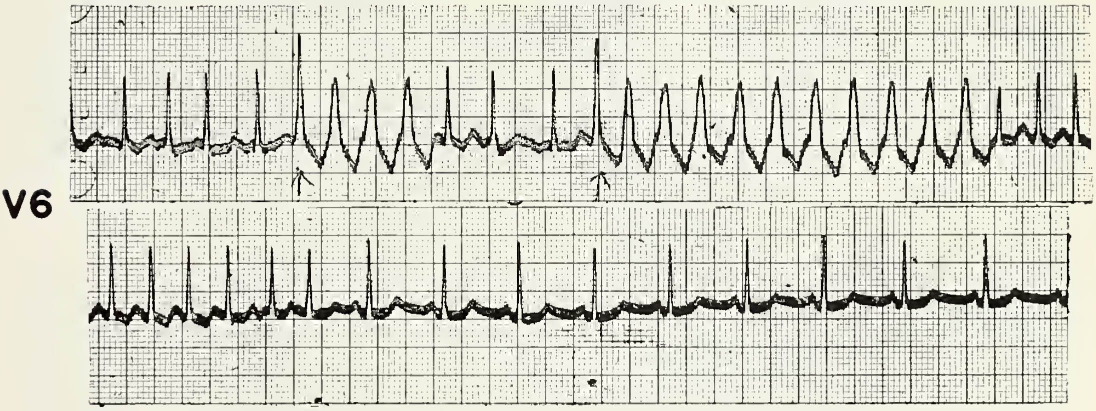
CONTROL



LEFT CAROTID COMPRESSION 10 SECONDS



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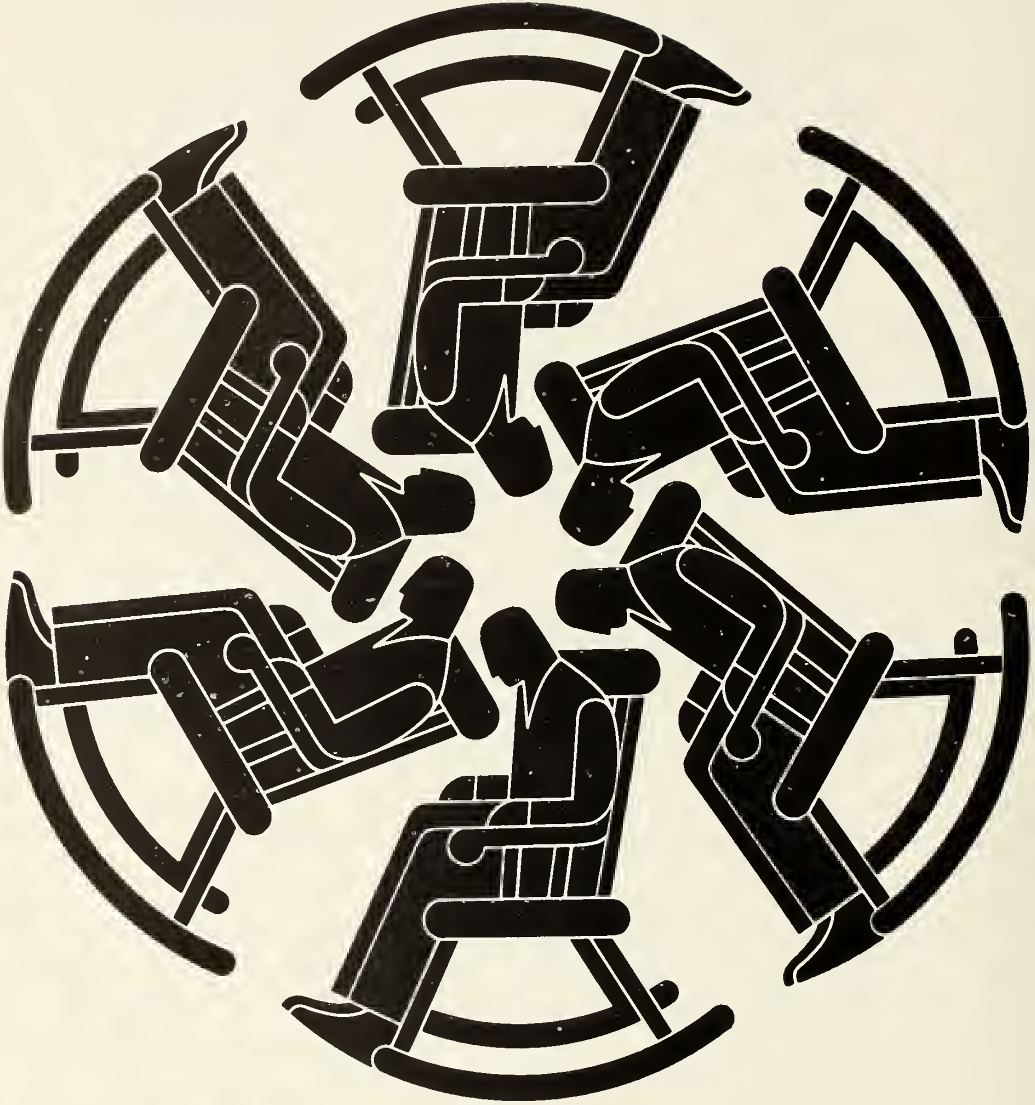

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Special Article

The Medical Profession and the Press

Paul Gough

Extensive mass media coverage of two issues during 1969 has probably been of great concern to the average physician. One is the abortive appointment of Dr. John Knowles to the post of assistant Secretary of Health, Education and Welfare, while the other involves reporting of income derived from goverment sponsored health care programs.

A recent editorial page commentary in the American Medical News, reprinted from the San Francisco Medical Society Bulletin reacted to the reporting of one such issue:[1]

"With so much amiss in the world, even in an age of provocative journalism, why do the propaganda media, and especially the newspapers, seem to wage such a vicious campaign against physicians? . . . .

"What propells the press to publish banner headlines teling of 'bonanzas' reaped by heart surgery teams out of welfare appropriations? Who sleeps at the switch? Who unleashes the dogs?

"Were these unusual instances of undisguised attacks against the medical profession and against the physician as an individual, it might be difficult to separate fact from paranoia. So numerous and frequent are the assaults in recent months, however, that some sort of design emerges, or at least a symbolic washing of the hands. . . .

"We may be witnessing the prodromal signs of an exploitation that would destroy the public confidence in the doctor of medicine for many years. We may be witnessing by the same token the exploitation of the press from within by a discontented few. . . ."

"Most editors are unaffected by statements like this, fortunately for the physician, since many newspapers are on the American Medical News mailing list. Words such as these will not, however, solve the problem. In fact, if there is a conspiracy, the conspirators would probably be encouraged by this type of reaction.

Less conflict and more contact may lead to a better understanding of the media, how the press gathers news, how one may react to statements and stories appearing in newspapers, and finally, how to keep the media better informed as to what is happening within the medical profession.

News about medicaid payments and the Knowles affair can be best classified as political, rather than scientific. It will appear whether the physician cooperates or not. Silence may be golden, yet it does not help explain an issue to the public.

To be fair, news coverage must encompass both sides of a controversial issue. In doing this, the reader can decide which he wants to believe. Also, since most of the action in the Knowles dispute was was either in Washington, Chicago or Boston, most newspapers had to depend on wire services and other such news sources for their information.

The second problem promises to be a perennial issue: publication of payments made to doctors under welfare programs. No one likes to see their income published, yet this information must be available when public money is involved. Stories such as these are released to the press by government agencies, not compiled by local newspapers.

In New York, statements have been made to the effect that up to $60 million in medicaid funds may have been wasted. Who made the charge? The mass media? No, it was a legislative committee, the media was only reporting on what the committee said.

By publishing a news story, a newspaper does not necessarily indicate that it endorses the point of view presented, it merely acknowledges the fact that something has happened, or a particular statement has been made. Except in the case of editorials, newspapers report on what others say, rather than what the publication believes.

The problem in understanding the media may be rooted in the traditional reluctance of the profession to become involved in public discussion. Long accustomed to working as a private practitioner or behind closed laboratory doors, it takes readjustment to get used to the idea that the public is interested and indeed wants to know what is happening in the field of health care. The average citizen pays the taxes that support these welfare and research programs, and is among the ones who

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MR. PAUL GOUGH is medical science editor for the New Haven Register, New Haven, Conn.

will ultimately benefit, so why shouldn't he be interested?

The press generally is not at fault when one side in a controversy feels its viewpoint is not adequately covered, it needs something to work with. Robert Slater, president of the John Hancock Mutual Life Insurance Company recently discussed the question:[2]

"With our nation in a state of alarming flux, responsible communicators face the challenge of adjusting themselves to reportage outside the spectacular and dramatically different. Although this is an age of specialization, it is also an age dependent on a wide range of knowledge. To convey such knowledge requires bridging huge voids between different habits of mind. And this is not the sole responsibility of the journalist.

"The press can only respond to what is made available. If members of industry, education, government or any field fail to supply the facts, then we have only oursleves to blame when we belatedly learn that our standpoint suffers from credibility."

The role of the physician in coverage of medical news is encompassed within the meaning of Section 10 of the Principles of Medical Ethics:[3] "The honored ideals of the medical profession imply that the responsibilities of the physician extend not only to the individual, but also to society where these responsibilities deserve his interest and participation in activities which have the purpose of improving both the health and well-being of the individual and the community."

The Judicial Council of the AMA has construed Section 10[4] "as encouraging physicians to work with the communications media as an integral and important part of the principle of upholding the responsibility of the physician to society as a whole."

A good definition of news is that it is a change from existing conditions, the greater the change, the greater the news. Accidents, disturbances, discoveries, disruptions, corruption, the first, the last, the only and the millionth are also news.

A second element of news is immediacy. An event which happens today and is reported today is news, while the same event is stale as news if it occurred three days ago. An exception would be an event of extreme importance which was previously unreported.

Besides its own staff, a newspaper usually draws on many additional sources for news and information. Most subscribe to a number of the news services which supply news both by wire, and in the case of advance or undated material, by mail. Except for the opportunity to refuse to publish, local newspapers have little control over the content of such material.

Newspapers are interested in local news since readers want to hear about what happens in their area and how it relates to them. Basically, it is the job of the newsroom staff to find such news and write about it.

The larger the newspaper, generally the greater number of reporters on its staff and the more specialization. Three newspapers in Connecticut, *The New Haven Register,* the *Hartford Times* and the *Hartford Courant* have assigned reporters to the medical "beat." The medical writer is expected to keep abreast of happenings in the field, know the people to call when a question arises, and to cover any stories assigned by the editors, as well as search out stories on his own. On other papers, most items would be written by a reporter assigned to write on that particular topic that particular time.

The newspaper appeals to a general audience, and information must be presented to the reader in a form which is easily understood. A reporter must follow a particular style in writing for a newspaper. Briefly this means relatively short words, sentences and paragraphs. Stories too must be short, rarely exceeding three double-spaced typewritten pages.

If a physician is contacted by a representative of the press, he may ethically "provide appropriate information regarding important medical and public health matters which have been discussed during open medical meetings or in technical papers which have been published. . . ."[5] Says the judicial council.

"Scientific articles written concerning hospitals, clinics or laboratories which portray clinical facts and technics and which display appropriate illustrations may well have the commendable effect of inspiring public confidence in the procedure described. Articles should be prepared authoritatively and should utilize information supplied by the physician or physicians in charge with the sanction of appropriate associates," it added.

The Judicial Council suggests that each medical society appoint a communications committee or designate a responsible individual or individuals, "whose duty shall be to provide the communications media with accurate information on all medical matters of interest to the public. This information should be given freely." Most questions which are likely to be posed to the average physician are covered by the already mentioned guidelines, queries about ethics should be referred to the communications committee or the medical society's officials for an opinion, according to the council.

To be useful, a decision usually has to be made quickly or the matter will lose its news value. At most newspapers there can be a lapse of less than two hours from the time something is said until it appears in print. If a reporter calls and asks for comment on the medicaid earnings for 1970, the story will not be discarded if no comment is forthcoming, it will just be printed without it.

When being interviewed by a reporter, either by telephone, or in person, bear in mind that the audience is composed of laymen who are interested but probably have no specialized knowledge of the subject.

In writing for a journal or speaking to a group of physicians, technical terms are expected, while in a newspaper, the vocabulary must be as simple as possible, particularly in a scientific article. The reader is interested with what happened and how it bears upon him and others, not in reproducing the experiment or passing upon its validity.

The reporter is consulting the physician as an expert in the particular field. The doctor should take care to be sure that reporter understands the subject matter, and be willing to spell words or provide a synomyn if requested. Questions such as these are asked to insure accuracy and understanding.

Writers attempt to convey material in the words of the person who said them. It is easier to take notes when the speaker talks a little slower than conversational pace. Most reporters want to talk to the source directly, so keep this in mind when asked for an interview. He wants to talk to and quote the expert, not a spokesman.

If there is any approval needed for an interview, get it before the interview. If there are any questions to ask of the reporter, don't hesitate. It is best to discuss possible problems before the interview.

Once a story is written, it goes to an editor who decides when it will be published, on which page, and at what length. Reporters do not write headlines and rarely see them before they get into print. The story is also subject to final editing, either to clarify a point or make the story fit in a particular size space.

If an individual physician wishes to comment on any issue related to medicine, this is best accomplished through a letter to the editor. This means was endorsed in a commentary in the American Medical News which pointed out,[5] "the letters to the editor have been very cooperative." The writer suggested a review of the factual content with the head of the press committee or the executive secretary of the county medical association because this "might help generate more fact and less steam."[6] Many newspapers have limited the length of such letters to 250 words or less, and generally the briefer it is, the better its chances for publication.

The best medium from the standpoint of news would be through an official statement of the state, county or local medical society or one of its officials. The Judicial council suggests that "spokesmen should be empowered to give prompt and authoritative replies and a list should be issued which identifies them and discloses the manner in which they may be reached.[8]

"These spokesmen may be quoted by name and title. This should not be considered by their colleagues as seeking publicity, since it is in the best interest of the public and the profession,"[7] the council said. "The officers, committee chairmen, and designated spokesmen of medical societies should be available at all times to bonafide representatives of the communications media in order that authentic information may be obtained as soon as possible." Availability is important, and quick replies generally make the newspaper. A delay may mean a missed deadline in the case of a story to be published that day, or an apparent one sided story.

Physicians who feel that the medical profession is not getting proper coverage in their local paper perhaps should consider discussing the issue with the editor. This is best accomplished by those experienced somewhat with contacting the media and as representatives of the county, state or local society. A meeting such as this may turn up some surprising answers to the question why there is no coverage, or poor coverage of the doctor and his work.

It may be the newspaper doesn't know who to reach when it seeks spokesmen. Also, meetings, or guest speakers or special activities can't be covered by a newspaper unless it is notified about them. If there isn't anyone available to cover a meeting, perhaps the editor would be willing to publish a story if someone calls after the meeting and tells what happened. At least one physician in the state has been writing brief articles for his local newspaper, so it can be done. Maybe spokesmen don't return calls quickly enough to be of use. There may be more explanations, find out, and then do something about the problem.

Finally, if physicians stop overreacting to bad publicity, there could be more good publicity. Since the press responds to what is available, physicians must do their part to see that their viewpoint is presented. If they don't, no one else will.

Here are a few guidelines to follow in dealing with the press:

1. Keep the vocabulary simple. Readers rarely consult a dictionary when reading their paper. They are more likely to skip a word or stop reading an article when they encounter a technical term rather than look it up.

2. In discussing research or scientific findings, be prepared to answer the question "What does it mean?" Doctors have the knowledge necessary to interpret findings while the general public does not.

3. If you are called to comment on an issue, respond quickly or you may miss the opportunity.

4. Assume you may be quoted unless specified by the reporter beforehand. You might be identified as a spokesman, rather than by name in the case of a political story, while in scientific matters, the name is very important. If there are any questions about this, ask.

5. A reporter reports on statements of others. If his name runs with a story, it does not mean he endorses the material in it. Also, newspapers publish both sides in a controversial issue, so by publishing a story, a paper does not express an opinion.

6. The length of a story generally has nothing to do with its quality. The longer the story and the more technical it is, fewer persons will bother to read it.

References

1. American Medical News, American Medical Association, Chicago. Oct. 13, 1969, vol. 12 number 40. Pg. 4.
2. Text of speech as supplied by John Hancock Mutual Life Insurance Company. Reported in part in Editor and Publisher, Oct. 18, 1969.
3. Judicial Council Opinions and Reports, AMA, Chicago, 1969. Pg. VII.
4. ibid. Pg. 66.
5. AMA News, Oct. 13, 1969, Pg. 4.
6. ibid.
7. Judicial Council Opinions and Reports. Pg. 64.
8. ibid. Pg. 60.

Society-sponsored Overhead Expense Insurance Program

Group Insurers, Inc. has informed the Society's headquarters office that, effective March 1, 1970, two provisions for increased benefits will be added automatically for those already enrolled in the Program:

(1) Reduction of elimination (waiting) period from 15 days to 12 days.

(2) Extension of allowable partial disability period from 45 days to 90 days.

Also, a new option will increase the limit of coverage to $2,000 per month for those eligible on the basis of age.

In launching another enrollment drive currently, the administrators announce that the new provisions and option will apply to first-time subscribers as well as to present policyholders.

By The London Post

British National Health Services

Part IV

Ned Thomas

(This is the fourth of a series of six articles).

LONDON, England—Unlike its American counterpart, the British Medical Association (BMA) accepts the National Health Service in principle. At the same time, it supports the idea of private medicine as an alternative to a state monopoly.

While the vast majority of British doctors support the National Health Service, they feel that it needs improvement, says Anthony Thistlethwaite, chief press officer for the BMA.

In the "Report by BMA Council on the Administrative Structure of the National Health Service in England and Wales," dated Dec. 28, 1968, the BMA does not take issue with the objectives of the National Health Service, but rather with some specific aspects of how it is administered. BMA also voices concern over what the Government might do in the future to restrict doctors' freedom of action.

The BMA report says in part:

"It cannot be emphasized too strongly that the cardinal objective of the administration of the Health Service must be the well-being and proper care of the patient in the broadest sense."

It adds: "The primary concern of the family doctor is the service which he can provide for his patients and how best this can be improved."

Improvements recommended by the BMA include:

1—Steps to relieve the shortage of doctors in Great Britain. It favors the expansion of existing medical schools and the erection of new ones. The BMA feels that at least 1,000 additional new doctors should be added each year to cope with the country's needs.

(Currently, about 2,000 new doctors are graduating each year in Britain. The average British general practitioner sees about 2,500 patients a year. The BMA want to reduce the G.P.'s average load to about 2,000 patients per year.)

2—Better equipped hospitals, with more modern operating rooms. It is felt that with better and more modern equipment hospitals could get patients out faster and thus treat more of them in less time than they do now.

(The vast majority of hospitals in England and Wales were built during the Victorian Period, between 1850 and 1900. Even with the building of almost 20 new hospitals since the National Health Service came into existence, there are a total of about 450,000 hospital beds, which, it is felt, is inadequate. Furthermore, the BMA feels that the hospital building program projected for the next 30 years is inadequate.)

3—Better conditions for junior doctors working in hospitals. The BMA feels that this can be achieved by better training of doctors and better amenities for doctors living at hospitals so that fewer British doctors will want to emigrate to other countries in the future.

4—Unification of all medical services of the general practitioners, hospitals and the municipal medical services.

Currently, the doctors in these three units are not united in a cohesive unit and the BMA feels that it is affecting their efficiency. Furthermore, BMA feels that the Government is not making the best use of its doctors, hospitals and facilities. It is hoped that these will be dealt with when the Government presents its new reorganization plans or Green Paper by the end of the year.

The BMA has rejected the Government's first reorganization plan and has recommended in its council report that the Government's new revised plan include a group of 13 proposals. Among these are:

- That no change be made in the aministrative structure of the National Health Service that would affect: confidentiality between patient and doctor, a doctor's independence in clinical matters, a doctor's choice of areas in which he wants to practice and the right of doctors to remain wholly or partially outside the National Health Service;

MR. NED THOMAS is a science medical writer for the New Haven Register on leave.

- That the administration or financing of the health service not be transferrtd to local authorities;
- That medical supervision oversee all social work services and that public health doctors be assimilated into any new medical services;
- That doctors be adequately represented in all levels of planning and administrative units and that the community be represented in the latter;
- That there be adequate provision for medical education and research, particularly in areas where medical schools are located;
- That the chief administrative officer must be medically qualified;
- That there be adequate financing of the National Health Service, and that separate provision for each branch of the service should be a prerequisite to any change in the administrative structure;
- That occupational health services should be included in any new administrative pattern for the National Health Service that may evolve;
- That the Government's main proposals enunciated in its Green Paper are unacceptable to the profession as a means of achieving unification of the National Health Service; and
- That any further discussions on possible changes in the administration of the National Health Service must take into account the principles set out in the Council's recommendations.

Representing the BMA's view, Mr. Thistlethwaite says that the people in England "could be suffering" as a result of shortages of medical staff, equipment, operating rooms and money, and the long term effect of inadequate medical training of junior hospital staff.

The BMA would like to see the Government pour more money each year into the National Health Service to improve it, but Mr. Thistlethwaite says the BMA is not prepared to say how much more this might require.

In addition, the BMA is concerned about the fact that about a half million persons needing non-emergency operations have been waiting for hospital beds in England and Wales from anywhere from several days to several years.

In view of the country's shortage of doctors, BMA is distressed that some 400 British doctors migrated to such places as the U.S., Canada and Australia last year. Mr. Thistlethwaite notes that this constitutes "a great problem" for the country. He adds it has been happening for the past 10 years.

While this number is made up many fold by young doctors coming to Great Britain each year from Commonwealth countries, BMA is concerned that many of these doctors do not have training equal to the jobs they are asked to do.

(The fifth report in the series, discusses the views of two general practitioners on the National Health Service.)

Summer Camp For Children With Learning Disabilities

A new summer day camp for children with learning disabilities will run from June 29th through August 14th. The camp will be held in Wilton.

In charge of the camp program is Mr. Geoffrey Beitner, a senior at William and Mary College. Assisting Mr. Beitner will be four assistants.

The camp will be limited to an enrollment of twenty youngsters. Minimum age is six years old.

For seven weeks there will be a Monday-Friday, half-day session from 9:30-12:30 P.M., and a half-day session from 1:00-4:00 P.M., Mondays to Fridays. Full day sessions will be held from 9:30-4:00 P.M. five days a week.

The morning session will provide the youngsters with bowling, miniature golf, picnics while afternoons will enable the youngsters to develop motor skills, swimming instruction, field trips.

For further information, call Mrs. Fred Wetzler in Weston at 226-0670 or inquiries may be made at the office of CACLD (Conn. Association for Children with Learning Difficulties) in Norwalk, Monday, Wednesday or Friday mornings (Telephone: 838-5010).

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SO YOU MARRIED A DOCTOR

"Medicine is a demanding mistress," said Sir William Osler. He chose his words with his usual discernment. This truth invariably comes as a shock to a doctor and his bride. To begin with let's look at the kind of man you chose to share your joys and burdens. This man is of a highly select group in the population. His IQ is high, averaging 125. He is high in drive, in energy and in motivation; he has an unusual ability to analyze and solve problems.

With these attributes this man becomes an individual holding a societal status just behind that of a justice of the Supreme Court. He is a high income earner largely because he was willing to make an extraordinary commitment both to his training and to his work. The doctor is a public man, a highly privileged and esteemed person who holds such usable keys as there are to happiness, health and life itself. For him society nullifies its rules and gives him freedom of action matched only by the responsibilities he assumes. How can a wife manage to live around such a ponderous image? From a purely theoretical point of view marriage to such a paragon seems a near impossibility. If the characteristics of the wives of the doctors were not so closely matched themselves, it would be unmitigated disaster!

The Basic Family Pattern

Whether the marriage begins before medical school, at internship or residency a common pattern is evident. The school, the hospital, the practice, sustains the No. 1 position in the life of the doctor. The wife, and later the children, are firmly placed in the No. 2 spot. This tends to persist as a habit pattern of living. It does a great deal of mischief. The divorce rate is smaller than average, but the overall quality is not high. The five most easily distinguishable kinds of relationships are described with great insight by John Cuber who began professional marriage counseling in this country.

The conflict habituated marriage

The couple establishes an early pattern of conflict and keeps it up as a way of living. Each subject becomes a contest or duel.

The passive-congenial marriage

The couple married to be married and never have either a warm or a conflicting relationship. These people are the mainstem of civic activities.

The devitalized marriage

This is the great mass of marriage, revolving around maintenance of a house, raising children and no longer having anything to say to each other.

Vital marriage

This is one in which the pair manages to meet most of the other's needs. They are often relatively nonsocial and looked upon with suspicion.

Total marriage

The couple are entirely wrapped up in each other, tending to appear anti-social. They are usually actively disliked by their cohorts.

What are some of the special personally difficulties characteristic of doctors? There are three which can play havoc in the marital picture.

Communication failure. Men as a group have more trouble with this than women. Women talk more, faster, longer and better than men. One of the cultural sterotypes links strength with silence. Professionally, the doctor has to be careful of any warm expressions because it tends to draw patients in too close to his professional image shield. So the doctor necessarily learns to wear the cloak of detachment. He is often too quiet at home for his wife's comfort.

Conflict-avoidance. The doctor is unaccustomed to sustaining conflict. In contact with other doctors

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differences of opinion are minimized amounting to a kind of professional etiquette. Where conflict arises with his patient, he seeks either a quick resolution of it or quickly suggests the patient get himself another doctor. This habit pattern carried over to the home tends to produce equally long-term smouldering conflict which is very destructive.

Smothered dependency need. Few things annoy a woman more than to meet a man who is happy and independent and doesn't need her. This sounds like the appearance of most of the doctors. It is an erroneous view. Within the image of the doctor dwells the mere man. The endless patients heap upon this image their lives, cares, problems and diseases. He bears a vast burden alone. The little boy who had to tell his mother his problems has grown to be a doctor. He ought to be able to tell his wife—but he rarely can. So he has what the psychiatrists recognize as an unmet dependency need.

Here are some tragic facts. Doctors form the largest single group of hard narcotic users, and one of the largest groups of habitual users of amphetamines and barbiturates. Doctors form one of the largest groups of professional people suffering from chronic alcoholism. They are often hard drinkers. Suicide appears to be an extraordinarily high risk for the doctor. A better ability to express their dependency need, and to have it truly met—preferably by their mates—would surely make a drastic reduction in those cold statistics of personal tragedy. How fares the doctor's wife? Because the doctor has difficulty in communicating his feelings the wife tends to lack feelings of worth in the face of the ever-present though erroneous—doctor image. She tends to misinterpret his inability to communicate as his self-superiority. So she feels left out and unwanted. At the same time she is aware of the fact that she has had to undertake a major portion of the management of the home. Because of the similarity of personality types between doctors and their wives, the wife has the individual strength equal to her daily tasks. She herself is an unusually able person. Frequently, before her marriage, she was an unusual accomplisher herself. She then requires something in the way of an achievement beyond that of wife, or mother. The wife and children are very apt to be both physically and mentally poorly cared for. The effects of this on the doctor's wife are much like those on the doctor himself. Admissions to mental hospitals are about twice as frequent among doctor's wives as in the comparable middle-class segment of the population as a whole. Most of these unhealthy, unpleasant characteristics can be remedied. With all its hazards, a medical marriage can still be a good one. Each of us has the power to change that within ourselves which is destructive to the wholeness of marriage. We change when we show to the other persistent and continuing interest, concern and understanding. Husbands and wives, if the marriage is to truly successful, must meet each other's needs for attention, approval and love. Each partner must be the guardian of the dignity and be privacy of the other. Only if we are conscious of these things can they come to pass. But if we bring them to pass, we will have achieved the head-to-head intimacy that was so briefly ours in the courting ear.

This article is based on an address delivered at the AMA Woman's Auxiliary Fall Conference, September 1968 by Joseph B. Trainer, M.D.

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Index to Advertisers

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Burroughs-Wellcome, Tuckahoe, New York	bet 228 & 229
Campbell Soup Company, Camden, N.J.	bet 260 & 261
Dentocain Co., Bloomfield, Conn.	226
Dow Chemical Co., Midland, Michigan	bet 277 & 278
Arthur W. Eade, Hamden, Conn.	294
Geigy Pharmaceuticals, Ardsley, N.Y.	bet 228 & 229, 229
Geriatric Pharmaceutical Corp., Floral Park, N.Y.	275
Glenbrook Laboratories, New York, N.Y.	225
Group Insurers, Inc., New Haven, Conn.	281
Hynson, Westcott & Dunning, Inc., Baltimore, Md.	3
Lederle Laboratories, Pearl River, N.Y.	5
Eli Lilly & Co., Indianapolis, Ind.	FC & 10
McNeil Laboratories, Inc., Fort Washington, Pa.	223
National Drug Co., Philadelphia, Pa.	2, bet 244 & 245
New Britain National Bank, New Britain, Conn.	231
Poythress, Wm. P., Richmond, Va.	bet 228 & 229
Responsive Data Processing, Corp., Mount Kisco, N.Y.	IBC
Robins, Co., A. H., Inc., Richmond, Va.	240, bet 260 & 261, bet 277 & 278, bet 292 & 293
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Smith, Kline & French Laboratories, Phila., Pa.	9

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Richard Quintiliani, M.D., Guest Editor

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CONTENTS

editorials

Cleaning Up Our Environment: Steps Taken To Abate Air And Water Pollution . . . 297
Unheard Voices Of Surgeons In Britain . . . 298
Physiologic Changes During Transcendental Meditation . . 302
Idoxuridine (IDU) In Herpesvirus Hominis Encephalitis . . 303
Isometric Exercises And Physical Fitness . . . 304
Clinical Implications Of The Sleep Cycles . . . 307
When Is Rheumatoid Arthritis, Rheumatoid Arthritis . . . 312
Circadian Rhythms In Man . . . 314
Differences In Patterns Of Surgical Practice . . . 316
Some Consequences Of Chemical And Biological Warfare . . 318

scientific

Foreword, *Richard Quintiliani, M.D., Guest Editor* 320
The Intrathecal And Intraventricular Administration Of Antibiotics In Central Nervous System Infections, *Richard Quintiliani, M.D.* . . . 321
Endocarditis In The Drug User, *Vincent T. Andriole, M.D.* . 327
Adrenocorticosteroid Therapy Of Bacterial Meningitis, *George F. Thornton, M.D.* . . . 331
Vaccination Against Meningococcal Meningitis, *Irving Goldschneider, M.D.* . . . 335
Rubella Vaccine—Some Perspectives, *Martha L. Lepow, M.D.* 340
Infection Of The Urinary Tract, *George W. Lewis, M.D.* . . 343
Usefulness Of Gram Stain And Routine And Quantitative Culture Of Sputum In Patients With And Without Acute Respiratory Infection, *Raymond C. Bartlett, M.D.* and *Avrohm Melnick* . . . 347

departments

The President's Page . . . 354
From The Executive Director's Office . . . 355
Physician's Placement Service . . . 358
Woman's Auxiliary . . . 378

miscellaneous

Electrocardiogram Of The Month, *Hyman N. Chernoff, M.D.* 362
British National Health Services, *Ned Thomas* . . . 365
Law-Medicine Notes, *J. Alfred Fabro, M.D.* . . . 367
New Books Received . . . 369
From the Connecticut Regional Medical Program, *Henry T. Clark, Jr., M.D.* . . . 370
Around The State . . . 373
Meetings . . . 376
Doctor's Office . . . 376
Letters-To-The-Editor . . . 377
Obituary:
Samuel Jaffe, M.D. . . . 379
In Memoriam . . . 379
Science News . . . 381

Connecticut Medicine

editorials

Cleaning Up Our Environment: Steps Taken To Abate Air And Water Pollution

The ponderous machinery of government is beginning to move, and industry is behaving as if they realize that they cannot go on increasingly polluting the air.[1] The automobile manufacturers now know the nuisance they are creating and are beginning to take action against it. In California this year, new cars will emit 23 per cent less hydrocarbons than the earlier uncontrolled models. In the next year, the California standards will apply nationwide to new models.

General Motors has committed itself "to take the automobile out of the smog problem altogether." Recently Secretary Finch issued a schedule for reducing the permissible limits of pollutants from the combustion engine. By 1975 the emission of hydrocarbons is to drop to about 5 per cent of that of uncontrolled vehicles. Next year's models will emit about one third as much carbon monoxide as the uncontrolled car.

Control of nitrogen oxide however has lagged behind, but California standards require a partial abatement in the 1971 model year. The federal standards for 1975 call for a substantial change—a drop to about 15 per cent of present levels. A striking feature of the abatement of motor vehicle pollution is its price. The improvements incorporated in the 1971 models will cost no more than $48 per vehicle.

In terms of tonnage of emitted pollutants, the auto ranks first. However, in overall damaging effects, sulfur oxides from burning of fuels seem most serious. This is especially true in the area east of the Mississippi and north of the Ohio, where sulfur-bearing coal is a principal fuel. In that region, major metropolitan areas have been gambling with disaster. An unusual weather pattern with a persistent inversion could result in many deaths. In November 1966, the New York metropolitan area came close to such an event.[1] The experience caused authorities in the area to issue regulations calling for progressively improved control of sulfur oxides. In abating its air pollution, New York in effect limited the sulfur content of fuel to 1 per cent.

As a result, the concentration of atmospheric sulfur oxides is now less than half what it was in 1966. During 1971 the permissable sulfur content of fuel for most installations will drop to 0.37 per cent. This will reduce air pollution further. It will also have substantial economic consequences. Fuel will cost more. It will consist mainly of natural gas, purified residual oil, and clean fuel oil.

It is said that this country "cannot afford" to import enough low-sulfur oil to meet its energy needs. This sounds hollow when 130 billion is being spent on war and allied activities. Until we change our ideas on priorities in many regions, it will be necessary to use coal which typically contains 2 to 3 per cent of sulfur. Only a small fraction of the reserves contains as little as 1 per cent. It is possible to remove some of the sulfur from coal by mechanical means, but most cannot be eliminated except by costly chemical processing. In major installations abatement of pollu-

THE COVER

PARÉ: SURGERY ACQUIRES STATURE

AMBROISE PARÉ, young French army surgeon with troops of King Francois at Turin, in 1536, had his first experience treating men for arquebus wounds. Running out of boiling oil (traditional treatment for gunshot injuries), he improvised, discovered that unburned patients healed much better, and resolved never to use hot oil again. It was some years later, in 1552, that Paré put aside cautery irons used to stop bleeding in amputations and reintroduced ligatures for tying bood vessels. During his life (1510-1590), practical, inventive, observant, compassionate Paré served as surgeon to four French kings; earned the title: "Father of Surgery."

tion arising from the burning of coal will require cleansing of stack gases.

At a recent congressional hearing,[2] four processes were described that have reached the stage of commercial application. They are all capable of sharply reducing the concentration of sulfur oxides emitted by major electric power generation stations. The using public will naturally have to pay more for his electricity—from 6 to 10 per cent more, according to present estimates. In view of the health hazards and other costs of pollution this seems a small price to pay. With this new technology the major polluters can lower their emissions of sulfur oxides, and they should be required to do so now.

Restoring the quality of the air we breathe is only one of the environmental problems. Another is restoring the quality of our water resources.[3] In contrast to the technology being developed in abating air pollution, the technics of treating municipal wastes were those of 50 years ago until very recently. First they removed mechanical solids, then there was a secondary treatment to accelerate oxidation of organic matter. The processes were less effective in reducing the level of fixed nitrogen, phosphate and intractable organic chemicals. Now we know this was not enough and in addition, there has been growing concern about the numerous organic chemicals that are finding their way into streams and lakes.

At long last some imaginative engineers have turned their attention to the problem. What can be done is illustrated by a new plant at Lake Tahoe.[4] Processing there results in reduction by 99.3 per cent of biochemical oxygen demands and the removal of 94 per cent of phosphates and 99.99 per cent of coliform bacilli. Included among the steps are a flocculation at pH 11.5-12 with lime, adjustment of pH with CO_2 and a final polishing of the effluent with activated charcoal. The effiuent is then pumped from the Tahoe basin into another valley where it is stored for irrigation in a man made lake where trout thrive. The citizens at Lake Tahoe were highly motivated and were willing to spend heavily to save their beautiful lake.

However, citizens elsewhere have not been so effective. Communities have refused to tax themselves to provide benefits for down stream users. Authorities have been reluctant to interfere with industrial pollution, fearing loss of local industry. The federal government has functioned poorly. After more than 15 years, the federal water pollution program has not yet brought about significant improvement in any major water course. A recent government report[5] states "Federal grants have been awarded for construction of facilities which provide treatment for only part of the pollutants discharged into waterways, nearby municipalities or industries have continued to discharge untreated or inadequately treated wastes."

With a great show of unanimity and self-praise, Congress passed the Federal Water Pollution Control Act of 1965. The act authorized substantial appropriations for grants for cleanup. The real point was that Congress refused to appropriate more then trifling sums for the purpose. Last year. they appropriated more but even these cover only roughly half the costs of projects and much foot-dragging can be expected. Cleaning up the rivers and lakes in this country will require good technology that we have, and good politics that we don't have. Until we have both good technology and good politics, needed actions to improve our environment will not be taken. But action must be taken now if we are to achieve an optimum balance of man and nature on this magnificent but imperiled planet.

L.H.N.

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Unheard Voices Of Surgeons In Britain

Hospital junior staffs in Britain put up with long hours, poor pay and little formal training because they thought a consultant pool worth getting. Riddell[1] studied the fate of such juniors as they are called registrars in South Wales-Western regions. Once they have taken a registrarship in surgery, they are committed to surgery as a career. Consequently, if one fails to obtain promotion in the health service he emigrates rather than go into general practice.

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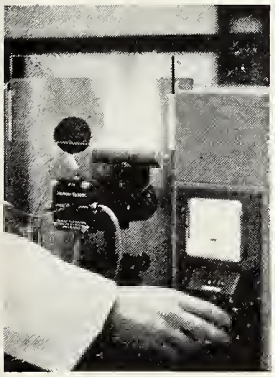

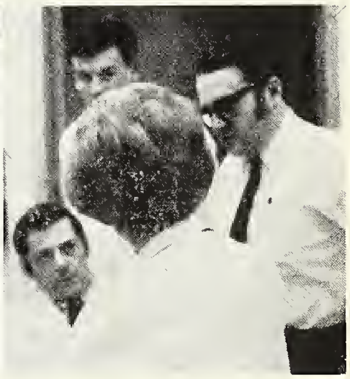

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In 1964, it was estimated that one fourth of the total British graduates emigrate. Forty out of 100 emigrants gave as their reason, better opportunities abroad. Riddell's group left the country not because they wished to practice abroad, but rather because career prospects in Britain are poor. They were able well-trained highly motivated who had persisted in following a surgical career rather than change the pattern of their career. They emigrate owing to lack of future opportunities.

How does the physician feel who succeeds in becoming a consultant surgeon? He sees his private patients quickly and operates on them quickly. He thinks it is the National Health Service (NHS) with its delays and frustrations that needed changing and not his private practice which is at it should be. He had only a few private patients, two-three new ones a week and perhaps one operation. But for this work he earned as much as from his operating lists, outpatient sessions, his ward rounds, teaching, and his home visits for the NHS. For his NHS he was paid less than $10,000 per year.

He believes that in a society which equates salary with esteem and worth to the community, consultants are grossly undervalued. It was because he was underpaid for the work he did for the NHS that Dr. X resented the bland way in which extra demands were made on his time by postgraduate lectures and the numerous committees, planning, staffing, teaching and so on. He did not so much feel overworked as exploited. He did more emergency work because he was recently appointed. His routine lists—five a week were major operations. All varicose veins, hernias, etc. were channeled to a surgeon at a small hospital 20 miles away and the waiting list was four to six weeks.

The average working day lasted from 9:00 A.M. to 6:30 P.M. and this included each week two-three teaching sessions at lunch time in the postgraduate center. The committees took up a lot of time not only attending them but reading through the masses of paper work at home in the evenings. However, his weekends were free, three out of four.

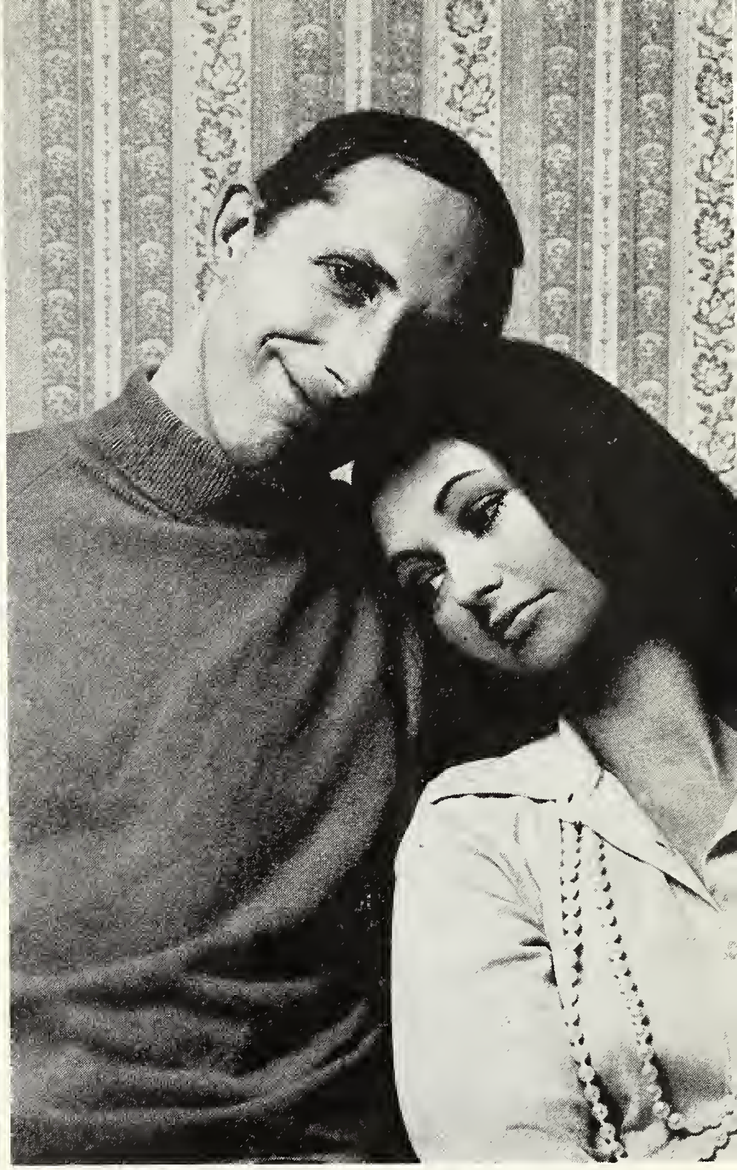
The patients, however, really got a raw deal. The hospital buildings were old, ill fitted for modern surgery and in poor condition. The outpatient waiting hall, for example, he thought "disgusting". Although the appointment system worked well there was a delay of up to 6 weeks for a new patient to be seen, but once seen he could be admitted within a month if he needed an operation although this delay depended on the number of emergencies.

The operating rooms were "awful". There was no forced ventilation and the temperature in the summer under the lamp had been 100°. His Ganaian house officer said that in Gana all operating rooms are air conditioned; The operating room corridors had been used as a thoroughfare for visitors and this was changed after 8 years of protest. The wards too were depressing, long bleak barracks with no privacy, primitive sanitation and constant noise. They won't change it because a redesign would require more nurses which they do not have.

Time and again deficiencies were explainable solely by shortage of money. A new hospital was being designed as a single story with miles of corridors, vast distances between the departments, cheap to build but inefficient and frustrating to work in. Dr. X speaks of the regional board 40 miles away out of touch and its staff, armed with "invincible ignorance". They were sure they knew how to design a hospital and that hospital staff had nothing to offer in the way of advice. It is Dr. X's impression that many of the non-medical staff are second-rate which is not surprising when you look at their pay scales. He believes the medical staff also has little "administrative ability". Both at regional board and lower levels, the administrators seemed to lack any spontaneity or drive, they never identified or corrected defects unless these were pointed out to them.

Apart from the consequences of financial starvation was there anything else wrong. The living quarters of the house staff were "disgraceful". Furthermore, it seemed only just that a consultant in one of the competitive specialties with long arduous training should be paid more than one in a less demanding field. He felt lucky, however, since he always had good applicants for his own junior appointments. Other specialties were not so fortunate and he found the staffing of the emergency department was always a headache.

One thing saddened him since the introduction of better off-duty for junior staff, their sense of commitment to their patients declined. He could not understand how a good registrar could let someone on another team operate on one of his patients, when he was in the hospital even if he was off-duty. Such is the price of progress.



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Clearly what the doctors want is to be given adequate time, staff and equipment to get on with the work they were trained for and to be paid a fair rate for it. Their disenchantment stems from their growing conviction that any reform will not achieve this.

L.H.N.

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Physiologic Changes During Transcendental Meditation

Philosophers have held for ages that it is possible for man to attain "higher" states of consciousness through meditation technics. At last this problem is coming under investigation through recording certain physiological changes that take place during some of these practices. If there are such changes, they might even have some practical applications.

Studies in India about some autonomic functions in "practitioners of Yogi" showed a lower breath rate, an increase in skin resistance, but no consistent changes in heart rate or blood pressure during various yogi practices. The real problem, of course, is to find expert practitioners of Yogi so that measurements might be made in a way that did not interfere with the subjects' contemplative or concentrative efforts.

Wallace[1] found a large number of subjects readily available who had received consistent and uniform instruction through an organization that specializes in teaching this technic. He was interested to find out whether the practitioners immediately experience beneficial physiologic changes as claimed. Do the subjects during the experiment find it just as easy, enjoyable not involving concentration or contemplation or any type of control?

The technic is defined as "turning the attention inwards towards the subtler levels of a thought until the mind transcends the experience of the subtlest state of the thought and arrives at the source of the thought". There is no suggestion, mental control, or physical manipulation involved in the technic. The instruction is given personally by a teacher qualified by Maharishi Mahesh Yogi.[2] The technic is normally practiced twice a day for periods of 15-20 minutes. During the practice the subject sits in a comfortable position with the eyes closed.

Wallace[1] chose 15 "normal" college students experienced in Yogi, that is with no mental or physical disability. Each subject sits quietly with eyes open for 5 minutes, then with eyes closed for 15 minutes. Then he meditated for 30 minutes while continuing to sit with eyes closed for another 10 minutes. Finally, he opens his eyes and sits for 5 more minutes. Oxygen consumption was properly measured, so was the skin resistance, the electrocardiogram and the electroencephalogram.

Within 5 minutes the oxygen consumption dropped 20 per cent, remained low during the meditation and returned to normal after the meditation. Skin resistance increased markedly at the onset of meditation and also decreased to normal after meditation. The heart rate decreased but slightly during the period of meditation. There were also specific electroencephalographic changes quite different from that during sleep.

During sleep there is also a decrease in metabolic rate. However, the pattern of skin resistance is less than during meditation. The physiological state attained in transcendental meditation also appears to be different than during hypnosis or autosuggestion. The hypnotic state does not noticeably change oxygen consumption nor is there any EEG change during hypnosis.

Conditioning can alter autonomic function and EEG patterns. A subject can increase his alpha-wave activity through auditory and visual feedback. It has also been shown by instrumental technics that animals can learn to control their heart rate, blood pressure, and some endocrine secretions. Studies on human subjects reveal that heart rate, skin resistance and blood pressure can also be controlled. However, the practical application of such procedures needs further investigation.

Expert practitioners of some meditation processes have been found to have some control over involuntary physiological functions. Some of these changes could have practical application. Studies in this area have been negligible, however, owing to the difficulty and impracticability of teaching these processes. The fact that transcendental meditation is easily learned and produces significant physiological changes in both beginners and advanced students gives it certain advantages over other more austere technics. Physiologically, the state produced by transcendental meditation seems to be distinct from the commonly encountered states of consciousness, such as wakefulness, sleep, and dreaming, as well as from altered states of consciousness, such as hypnosis and autosuggestion.

Subjective reports as well as the objective data obtained from physiological measurements suggest that this state might have applications to clinical medicine. Transcendental meditation has been reported to have practical therapeutic value in relieving mental and physical tension. These reports are consistent with Wallace's findings in his subjects. Its value in the alleviation of drug abuse has been suggested. Its value in controlling arterial pressure is under investigation now.

There also may be other applications in those states where there are extended periods of low oxygen consumption as in space travel and low oxygen supply to the brain.

L.H.N.

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Idoxuridine (IDU) In Herpesvirus Hominis Encephalitis

Herpesvirus hominis is the most frequent and devastating of acute viral infections of the brain in the United States today. Its real incidence remains unknown. Some patients with encephalitis due to herpes simplex have prolonged courses that are difficult to distinguish from those of other patients with subacute sclerosing panencephalitis. Measles virus has been isolated from brains of several of these patients and there are high titres of measles antibodies in serum and spinal fluid. On the other hand antiherpes virus antibodies were not present in the spinal fluids in Nolan's series of 13 patients.[1]

Untreated the mortality is very high and morbidity almost total in the recovered patients. Olson[2] reported 69.5 per cent mortality among 36 patients with H hominis encephalitis and only 3 of the 36 had no residua. In Nolan's series four of six patients with a similarly grave illness survived and are intact after intravenous idoxuridine. These data are highly suggestive that this drug is effective therapy for severe herpesvirus encephalitis.

Until the introduction of idoxuridine disappointingly little has been accomplished in the development of anti-viral chemotherapy, although great strides have been made in the development of virus vaccines against some of the major epidemics in man. There are many serious viral illnesses that are not preventable by vaccination and such a disease is herpes virus encephalitis. It is the most sporadic fatal encephalitis in this country.

The illness is characterized by rapid onset a high frequency of focal seizures regardless of age of the patient, bizarre behavior, hallucinations and unusually severe clinical disease during the acute stage. Cutaneous herpetic lesions are not found in most patients and cerebrospinal fluid may be normal. The diagnosis can be confirmed by needle biopsy of the brain for virus isolation and for examination for nuclear inclusions or for specific herpes virus antigen by fluorescent technics.

In 1966 Breeden, et al[3] used IDU in a 34 year old man with herpes virus encephalitis. Since then several case reports followed but different quantities of the drug were administered at different single stages of the illness with expected variable results. But the striking thing about these case reports is that each patient survived the disease. Nolan's series is the largest to date in the treatment of herpes virus encephalitis and the fully treated cases recovered completely. The side effects included stomatitis, leukopenia, alopecia and in one patient loss of finger nails. All these abnormalities were reversible and secondary infections which were noted during the period of leukopenia yielded to antibiotic therapy.

Hanshaw[1] points out that Nolan's experience does not establish the efficacy of IDU in herpes encephalitis because of the small group randomly selected and because the diagnosis must be considered tentative in patients in whom the virus has not been demonstrated in affected brain tissue. Furthermore, fourfold antibody response alone may represent reactivation of a latent virus anywhere in the host and strongly support but do not prove that herpes virus is the cause of encephalitis.[4] Nevertheless, Nolan's report is clearly the most encouraging to date and should provide the impetus urgently needed for interested investigators to pool their experience in a controlled study much as cancer chemotherapy groups have done.

If herpes hominis replication can be inhibited it should become possible to control severe infections with related agents such as herpes varicella (varicella Zoster, cytomegalic virus and herpes virus semiae (B). In fact, Cangir et al[5] have reported clinical improvement in cytomegalovirus pneumonitis treated with a thymidine analogue floxuridine. These observations also require confirmation. There are recent indications that cytosine arabinoside, another compound with activity against DNA viruses may also prove useful in the treatment of severe varicella Zoster infections.[6] As yet the use of systemically administered inteferon inducers such as double stranded RNA (Poly 1-poly c) has not been reported in herpes encephalitis or other herpes virus infections in man.

Clearly we are rapidly approaching a period in which several antiviral substances are reaching a stage in development where trials on human beings with certain threatening viral diseases may be justified. This can be seen in the rapid expansion of knowledge of the phases in the sequence of viral replication. It is also now recognized that there were important differences between the metabolic requirements of the virus and host-cell. Finally are the encouraging results obtained in animal systems. These developments offer hope that therapy with antiviral agents are pharmacologically feasible.

There remain major obstacles to overcome, severe drug toxicity, possible developments of viral resistance. Then there are the teratogenic effects of powerful DNA inhibitors. Nevertheless, the prospects for future successful systemic therapy are brightened by Nolan's[7] studies which have brought us a step closer to realization of successful chemotherapy in serious viral infections.

L.H.N.

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Isometric Exercises And Physical Fitness

The obese, the infirm, the aged are unlikely to continue or undertake jogging before breakfast in order to achieve physical fitness. This has led some physicians and the open press to urge instead utilization of isometrics as a form of exercise to achieve physical fitness—press-ups, push-ups, and pull-ups. If we can use current advertisements as a measure of isometrics popularity, then the sale of a variety of devices for isometric exercises, which have become brisk indicates a growing popularity. Accordingly, we should know the physiologic responses to isometric exercise and thus be able to examine the case for or against this type of activity.

There are many kinds and degrees of static effort. Common examples are lifting or holding, carrying objects of all kinds, pushing furniture, opening doors or windows that are difficult to move. Working with the arms overhead is another common example since a good deal of static effort is needed to hold arms in position even before muscular activity or the weight of tools has been added. Lind[1] points out that isometric training does improve the strength of a muscle group. However, there is strikingly little associated increase in aerobic capacity or cardiovascular efficiency and little contribution to fitness for sustained dynamic exercise.

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increase in heart rate or blood pressure. At higher tensions for example at 20 per cent of maximal capacity fatigue occurs rapidly and at 50 per cent maximal capacity fatigue of the muscles occurs in 1-2 minutes. However, even though the heart rate increase is modest both systolic and diastolic pressure increases dramatically and the mean pressure at the point of fatigue is 140 mg Hg or more. By contrast in fatiguing rhythmic exercises—a treadmill of progressive severity—it is the heart rate which increases while the mean blood pressure shows only slight changes. Thus, in isometric exercise we find a widespread peripheral vasoconstriction with a resultant increase in blood pressure.

The striking point is that the mass of skeletal muscle involved is within an extreme range unimportant. The relevant factor is the fraction of the maximum isometric tension exerted by any muscle group. For example a 30 per cent contraction of the small forearm muscle in a hand grip or a 30 per cent contraction of the large leg muscle pushing the knee up against an immovable force will each result in the same degree of pressor response even though the work in the arm muscles is less than 1/3 that in the leg muscles. If the arm and leg muscles contract simultanously at the same proportional tension, they do not have an additive effect and the pressor response remains the same as if only one of the groups of muscles had contracted.

An additional point of importance is that the pressor response to static effort is the same when the subject is seated as when he is already engaged in mild or rhythmic exercises. In this latter situation the increases in heart rate and blood pressure are simply superimposed on the existing responses to the dynamic work. The pressor response to isometric contraction is, therefore, powerful, and elicited alike from small or large groups of muscles and when the individual is otherwise at rest or when he is already active.

Such increases in blood pressure by isometrics could have both untoward consequences in some situations as well as beneficial ones in others. In patients with aneurysms or incompetent valves, isometrics may represent a potential risk. Patients with coronary artery insufficiency, angina pectoris is known to be dramatically precipitated in the patient who works with arms extended or elevated. Accordingly one could logically assume that an increased pressure load brought on by isometrics would be less well tolerated by patients with coronary artery disease or one with borderline hemodynamic function. However, this phenomenon needs more extensive study. It might even become a method of imposing a graded pressure load during evaluation of patients with cardiovascular disease.[3]

In addition to heart patients, the obese, the infirm, and the aged often have flabby untrained muscles which are less able proportionally to lift or support the body weight. Due partly to their weaker muscles and partly to the effects of gravity on relatively or actually greater limit or body weight, they would more likely have increments in blood pressure than the younger and more physically fit when they practice isometric exercises. This is particularly so if those exercises are based on lifting the whole or part of the body weight such as pressups or pull-ups.

Most of the recent popular articles urge the use of isometrics mainly in those groups of people known to be more likely to have actual or potential weaknesses in their cardiovascular systems. From what we know about the pressor effect of isometrics their employment could very well expose the patient who should not employ them. If there is one kind of exercise that does little to improve overall work performance or cardiovascular fitness it is isometrics.

There are also possible benefits in practicing isometrics by people who need not fear the pressor effects which, however, have not yet been fully explored or documented. For example, it is possible that for those who suffer transient postural dizziness, appropriate isometric exercise may help to mobilize cardiovascular responses, particularly by an increased blood pressure or by the mild generalized vasoconstriction in inactive tissues. The pilot who blacks out on high maneuvers simply because of a reduced hydrostatic cerebral blood pressure might find isometrics helpful.

One could further conjecture that an athlete seeking power for his final sprint might benefit from an increased perfusion pressure by isometric hand exercise. We do not, however, as yet know whether such beneficial effects exist. Lind's investigations now underway when completed should help provide answers to these questions.

L.H.N.

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Clinical Implications Of The Sleep Cycles

The modern explosion of descriptive information about sleep can be viewed as a function of technical development principally the development of the EEG and Polygraph. While our knowledge of sleep phenomena has expanded, we still do not know how or why sleep occurs. During sleep the brain and peripheral nervous system under its control undergo continuous oscillation with a period length of about 90 minutes in human adults. During the nondreaming phase of sleep the brain waves are slow and of high voltage much as they are in coma and the peripheral autonomic system as measured by heart rate and blood pressure are low and regular. In this period people are difficult to arouse and report, if anything, thoughtlike mental activity.

The peaks of the cycle are characterized by low-voltage fast brain waves as is found in the waking state, by irregular high levels of autonomic activity and rapid eye movements. The arousal threshold is variable and reports of hallucinoid dreaming are frequent and so the cycle is subdivided in stages according to the electrographic criteria and continuous records scored to yield reliable measures of duration and periodicity. The nondreaming part of sleeping has been termed VREM and Hobson[1] terms it S while the dreaming part has been termed REM or D sleep. The temporal elements of this cycle are remarkably constant in all mammals or individuals indicating sensitive and strict central control as with other metabolic cycles and rhythms.

There are many implications of this differentiation during sleep. One concerning mechanism is that part, if not all of sleep, is actively controlled by the nervous system and is not a passive process or simply the absence of wakefulness. The commonsense notion of sleep as rest through inactivity may prove valid for the musculature, but it cannot be the whole story. There is a dynamism in dreaming sleep that has general medical implications because it is a time of periodic stress for man, especially for the cardiovascular and respiratory symptoms. By producing lesions in the brain stem of cats, it was found that the biological clock that controls the sleep cycle is located in the pontine brain stem. The activity here controls the rate of cortical discharge which is higher in D sleep than S sleep. The cortical neurons are caused to fire in bursts. The spinal reflex activity varies dramatically with phases in the sleep cycle and is controlled by descending influences from the brainstem.

It is probably true that during sleep deprivation animals tend to overeat and become hypersexual. On the other hand animals and man who are subjected to moderate exercise show earlier, more intense and prolonged S sleep and this suggests that recovery from fatigue may be facilitated by this kind of sleep.[1] During the D phase of sleep, there appears to be regulation of neural excitability. We still need to know, however, why we awake at 7 A.M. and feel sleepy at 11 P.M. Sleep is evidently internally regulated and occurs with a high degree of independence of waking behavior. This fact suggests the idea of central control of the sleep mechanism.

There are important clinical implications of the intense autonomic activity characteristic of D sleep. It has now been clearly demonstrated that clinically important increases in blood pressure, respiratory rate,[1] gastric motility and acid secretion[2] occur in phase with the sleep cycle throughout the night. This belies the outward calm of the sleeping patient. Nocturnal angina,[3] asthmatic attacks,[4] and emphysematous anoxic attacks,[5] have all been shown to occur in association with sleep-cycle peaks. It is, therefore, probable that fatal cerebrovascular accidents, and myocardial infarctions may be precipitated by the autonomic storms of D sleep. Thus, the patient with a predisposition to any of these diseases is potentially at great risk during times when prompt medical care is least likely to be available. That is, owing to its power and synchronization "sleep may at once be killing the patient and drugging the doctor".

Appropriate responses to this danger requires pharmacologic manipulation of the sleep cycle as well as modification of the sleeping habits of the medical staff. With regard to the first approach the requirement is a sedative that does not suppress D sleep but rather reduces the hallucination phase of D sleep into more thoughtful types of dreaming. The barbiturates have been shown to do just that and probably are important in all patients acutely ill and likely to show ex-

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Hepatic Reactions: Rarely, toxic hepatitis and jaundice, including some fatal cases.
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Ear Reactions: Hearing disturbances, deafness, tinnitus.
Central Nervous System Reactions: Psychotic episodes, depersonalization, depression, coma, convulsions, peripheral neuropathy, drowsiness, mental confusion, lightheadedness, dizziness, headache.
Cardiovascular-Renal Reactions: Edema, elevation of blood pressure, hematuria.
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aggerated D phase of sleep. As far as house staff is concerned, the need is to provide an alert physician instead of a groggy one at a time of great risk to the patient. These are excellent reasons therefore, for abandoning the 36-hour duty stints by interns.

Sleep research seems to have had less consequence in the fields of neurology and psychiatry. However, it has clarified for the neurologist the sleep pathologies chiefly by more precise electrophysiologic definition. The narcolepsy syndrome may result from a disorder of sleep-cycle control mechanisms. All its manifestations occur only in association with D sleep and narcoleptic patients do have abnormal sleep cycles.[6] Drugs such as amphetamines which suppress D sleep are useful in the treatment of narcoleptic patients.

The conclusion of importance to the clinician about sleep is that its two phases serve different functions. The nondreaming portion helps to restore the musculature while the dreaming portion can be dangerous to hypertensives, coronary artery disease patients, emphysema and peptic ulcers. Overactivity of the autonomic system can be reduced by barbiturates and probably other sedatives, thereby reducing hallucinatory processes to more thoughtful ones and in the process overactive autonomic activity.

L.H.N.

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When Is Rheumatoid Arthritis, Rheumatoid Arthritis

It was recently estimated that 3,600,000 of the adult population of the United States have rheumatoid arthritis. These statistics were based on diagnostic criteria established by the American Rheumatism Association (ARA). Obviously the accuracy of these statistics would depend on the validity of the ARA criteria. These established a point system for morning stiffness, joint tenderness or pain on motion, soft-tissue swelling of one joint, soft tissue swelling of a second joint within 3 months, soft tissue swelling of symmetrical joints, subcutaneous nodules, X-ray changes and serum positive for rheumatoid factors.

Some of these points, however, can lead to disagreement among the investigators. For example the finding of soft tissue swelling long considered one of the most reliable signs of active synovitis proved to be the source of considerable variation between observers. When rheumatologists were asked to perform independent examinations on a haphazard sample of the population, the disagreement rate was 80 per cent for positive findings.[1] This was attributed to the high rate of disagreement in the interpretation of minimal changes. It could be possible, for example, that the frequency of soft tissue swelling, particularly in the knees and fingers of older and generally more obese women had been overstated in this and similar studies. Another possible source of error in the ARA criteria is that persons with degenerative joint disease were included as well as rheumatoid arthritis.

Because of these possible errors in the ARA criteria, more recently criteria for rheumatoid arthritis were adopted at the New York Symposium on Population Studies in the Rheumatic Diseases.[2] The New York criteria are a history of episodes of three painful limb joints, swelling, limitation, subluxation or ankylosis of 3 limb joints, X-ray changes and serum positive for rheumatoid factors. These are much more stringent standards for distinguishing rheumatoid arthritis. Both the ARA and the New York criteria rely on periarticular soft-tissue swelling and symmetrical involvement. However, they differ in that ARA recognizes painful joints and morning stiffiness, whereas the New York criteria consider limitation of motion, a positive finding and require hand, wrist, and foot involvement.

The study of the Sudbury, Massachusetts population for rheumatoid arthritis by Cathcart and O'Sullivan is interesting because they examined 4552 people from 15-75 years of age and classified them first according to ARA criteria and again according to the New York criteria. According to the ARA criteria, they found a total of 3.8 per cent of females and 1.3 per cent males which satisfied these criteria and they found the incidence is higher as age increases. According to the New York criteria for rheumatoid arthritis, the prevalence was much lower 0.55 per cent for males and 86 per cent of cases occurring over age 45.

The Sudbury data indicated that the higher prevalence of rheumatoid arthritis by ARA criteria was related to the greater frequency of the individual components of these criteria. Furthermore, the finding of soft-tissue swelling, long considered one of the most reliable signs of active synovitis, proved to be a source of considerable variation between observers. In Sudbury, radiologic evidence of degenerative disease in the hands was much greater in persons with the symtoms and signs that comprise the ARA criteria than in those without such findings.

Any comment on the higher prevalence rate by the ARA criteria must refer to their original form which specified that joint swelling must be of at least 6 weeks in definite rheumatoid arthritis, an impractical criterion which was later modified for population studies.[3] In this regard, one study showed that when a series of examinations was carried out on the same population over a one-year period, the problem with persistent joint swelling decreased steeply with time.[4] This, of course, suggests that rheumatoid arthritis is often a relatively benign disorder that is only occasionally disabling. Furthermore, the relatively large segment of the population satisfying three or more ARA criteria, but lacking the classical features of a symmetrical polyarthritis, may have included many of those with "subclinical" rheumatoid arthritis, who rarely consult a physician.

Thus we find that both ARA criteria and the New York criteria agreed that rheumatoid arthritis is uncommon below age 45. They disagreed widely on its frequency in the whole community. If we consider the high frequency of individual joint symptoms and signs, the difficulties in interpreting soft-tissue swelling, and the benign nature of the disease in many individuals, it is probable that the ARA criteria would be a better indicator

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of rheumatoid arthritis for the physician who sees such patients.

The absence of well substantiated criteria makes it essential to be cautious. Radiologic findings revealed many persons had degenerative joint disease rather than rheumatoid arthritis. If Cathcart and O'Sullivan will continue their prospective study in Sudbury, it should contribute to the solution of the problem, when is rheumatoid arthritis really rheumatoid arthritis.

L.H.N.

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Circadian Rhythms In Man

Man has daily rhythms of body temperature, excretion and many other functions. We now know these rhythms are driven from within by a clocklike mechanism. They are not simply a response to the environmental periodicities associated with the rotation of the earth to which all life on this planet is subjected and wherein it has evolved.

One characteristic of circadian rhythms is its closeness to a 24 hour period, although exact values differ among different species and also among different individuals even littermates. A second interesting property of rhythms is the near-temperature independence of the period of frequency. Most chemical and biological reactions are greater by a factor of 2-3 at a 10°C higher temperature. Biological clocks appear to be only slightly changed usually by less than 10 percent. In some the system can be slower at higher temperatures as for example the bioluminescence rhythm in the unicellular dinoflagellate gonyaulax.[1]

A third key feature of circadian rhythms is phase lability, notably to light. How this works has not been worked out. In bird rhythms it is probably due to an involvement of the pineal gland.

In man Aschoff[2] has tabulated some 50 functions that have been studied and shown to exhibit an autonomous circadian rhythm. They range from basic cellular and tissue phenomena to those that involve organ and organismal functions. In addition to temperature and excretory and activity rhythms, there are circadian rhythms of cell division, heart rate, serum content of specific substances. There are more elusive phenomena such as ability to estimate time or the error rate in problem solving which also exhibit a circadian periodicity.[1]

Of more applied importance are the recent studies which show that the response of the organism to diverse insults may be different at different times of the day. Many years ago Halberg[3] demonstrated that mice are far more susceptible to killing by ethanol at one time of the day than another. Similar results have been obtained with such agents as ouabain and endotoxin. At one time considerable doubt was expressed at the remarkable finding that whole-body irradiation is more effective in killing if applied at one time of the day than at another time. Now it appears well verified.[4] Similar rhythms in sensitivity are known in man, for example skin reactions to histamine.

Aschoff, et al studied human circadian rhythms by means of placing men in underground bunkers for weeks. These subjects exhibit circadian rhythms different in length from the 24-hour rhythms but only by an hour or two. However, after several days, the subject is out of phase with the external world but is completely unable to ascertain or sense it. They used light-dark cycles. When the subjects were brought back to normal they were 12 hours out of phase, and very uncomfortable for a period of several days, much as people become out of phase when travelling by jet over several time zones. There is now evidence that temperature cycles and social influences can act as phase givers also.

There are several contemporary situations in which we are required to establish an activity-rest cycle or schedule to which we subject an individual. In doing so, it would certainly be wise to evaluate the effects of the period of the cycle upon the circadian rhythm. This is surely true for shift workers in industry. We know that efficiency as well as accident and error rate of workers varies with the time of day, and it would be important to understand and define the best conditions and schedule for someone working during

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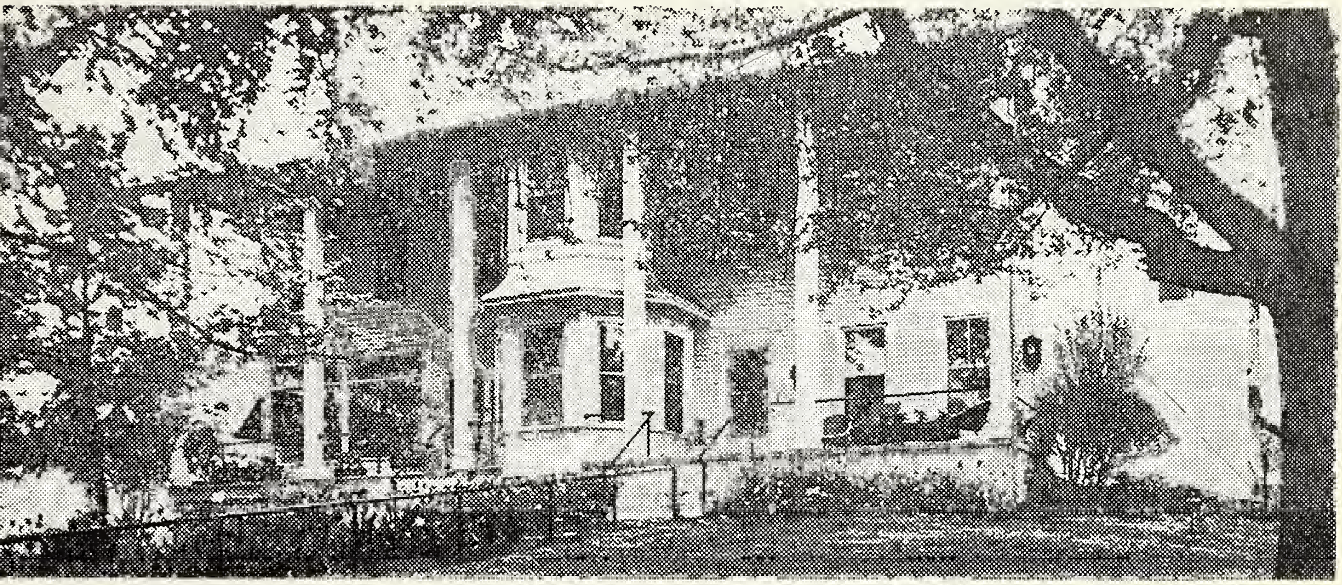

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the dead of night. Up to now, there seems to be no clear knowledge or agreement on this matter.

In the military the enlisted men on some submarines are apparently subjected to an 18-hour cycle (six on and 12 off)—an incredible six-hour phase shift each day. Basic studies on this kind of situation are urgently needed, since the officers on the same vessel reportedly live a 24-hour day. With such different shifts it would be difficult to obtain meaningful observations on possible entrainment and phase shifting of biologic rhythms.

Space flights, especially when carried out for extended periods, is yet another situation in which it will be very important to make careful evaluation and correct decisions on work-rest schedules for astronauts. This is especially needed because different rhythms may be dissociated-desynchronized. In Aschoff's underground bunker the activity rhythm may have a period different from the body-temperature cycle. This knowledge has immense practical importance. Within a few cycles the minimum in the temperature cycle may fall just 180° out of phase with the activity cycle. This renders the subject "physiologically upset".

A second quite different type of "desynchronization" has been reported. A few subjects in the bunker exhibit a natural period close to 48 hour rhythm rather than 24. They live a 48 hour rhythms without being aware of it. Emerging from the bunker after 20 days, they are convinced that only 10 days have elapsed. All activities are accordingly distributed within the 48-hour day—sleep for 16-20 hours followed by about 30 hours of activity; 3 meals a "day", etc.

One question is whether these rhythms have a molecular and cellular mechanism. Another question is whether there is a master-clock mechanism to which all the functions are tied or whether there is a multiplicity of clocks within the cell or organism. The cockroach very much like small mammals has an activity rhythm which resides in the subesophageal ganglion. Its removal abolishes the rhythm. But it can be restored by transplantation of the ganglion from a donor. However, now the activity rhythm is in phase with that of the donor. Thus, the nervous system seems to be the guiding hand in rhythms of lower animal forms and probably is the seat of the master clock which controls circadian rhythms in higher forms, including man.

L.H.N.

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Differences In Patterns Of Surgical Practice

Bunker[1] has recently presented evidence that serious maldistribution exists among surgeons and anesthesiologist in this country. There are now 9000 anesthesiologists as compared to 1000 in 1940. However, the magnitude of operations performed is such that anesthesiologist can provide anesthesia for less than half of the patients undergoing surgery and can hardly begin to offer anesthetic care for obstetrics and dental surgery.

The number of anesthesiologists in America per 100,000 is about the same as in England and Wales. But there are twice as many surgeons per 100,000 population 39 to 18 in England and Wales. There were 7400 operations per 100,000 performed in this country as compared to 3770 in England and Wales. This means that the anesthesiologist in this country has twice as much work to do as his British counterpart. Why are there twice as many surgeons and twice as many operations performed in this country than in Britain? In an attempt to answer this question Bunker considers effect of insurance in comparison with no insurance, prepaid in comparison with indemnity insurance, of group practice v.s. solo practice.[2-3]

Insurance, by itself, appears to increase the utilization of physicians' services, presumably in response to unmet needs. Group plans, however, such as the Health Insurance Plan (HIP) of New York and the Kaiser Foundation Health Plans, lead to approximately half as many operations. One explanation for this phenomenon is that intensive ambulatory care may lead to improvement in general health and hence to a decrease in need for hospitalization and surgery. One argument given is that in the absence of a fee, there is less incentive to perform procedures that are desirable but not absolutely necessary. Another possibility is that patients may accept group practice for routine care but go elsewhere when they need an operation. These apparently do not apply to HIP and neighborhood health centers for low-income families where the population could be closely controlled. It appears that the group-practice effect is what is reflected in a smaller proportion of surgeons as well as a smaller number of operations performed.

The British surgeon as a consultant is overworked and it is said there are long lists of elective cases that must wait interminally for operations particularly such as prostatectomy, herniorrhaphy and cataract. The British surgeon is modest in his expectations and perhaps missing opportunities for surgical care. The American surgeon appears more aggressive. He holds higher expectation of what surgery can offer in the treatment of disease. He performs more elective procedures. When given the choice of administering or withholding therapy, whether the therapy is prescribing drugs or performing an operation, the American physician appears likely to choose active therapy. The British surgeon carrying a heavier work load is apt to avoid surgery if the indication is in question.

Any decisions about how many surgeons we need in America must, of course, be based primarily on how much operative treatment the public requires. The fact that marked variability in surgical practices and presumably in surgical judgment and philosophy exists must be considered to reflect inadequate data by which to evaluate surgical treatment and specifically by which to compare operative with non operative treatment. Stated another way the indications for surgery are sufficiently imprecise to allow a 100 percent variation in rates of operation. The risk of operating can be documented with mortality data, but comparable controlled data on the risk of not operating are, for most surgical diseases, not available.[4,5]

This, of course, is one of the big problems nobody has ever bothered to work out, the natural history of any disease until what is regarded as an effective treatment has been found. Wide variations in surgical practices must have marked effects on the public health. For example, a hospital that reserves operative treatment for the very ill can be expected to report very different postoperative death rates than those in another hospital specializing in minimally indicated operations in good-risk patients.

Mortality data alone, however, cannot provide an adequate basis on which to judge surgical success or failure, or on which to define surgical indications and contraindications. Quantitative data on other important surgical end-result indexes, such as complications, rehabilitation and relief of discomfort are not available. Since direct measurement of the quality of medical care, by death rates is exceedingly difficult, studies of the quality of medical care have relied heavily on other kinds of information such as internal and external audits and the qualifications of the physician rendering care. It would seem that the surgical care rendered by prepaid group practice such as HIP and Kaiser Foundation was judged to be superior to that under the Blue Shield insurance plan.[6,7]

One factor reducing quality of surgical care in this country seems to be many hospitals do not require board certification or equivalent training. Of the 68,000 physicians listed in full-time or part-time private practice in surgery less than 2/3 are certified by a surgical board or are Fellows of the American College of Surgeons. There are no national data specifying who does the surgery in this country. It has been estimated that more than 50 percent is performed by general practitioners or osteopaths. Whether fairly or not, it is to the "unqualified" surgeon that most unnecessary operations are attributed.

The ratio of surgeons and of operations to population are half as large in certain group practices in the United States as in the country as a whole. This same ratio obtained in very large group practices as exists in England and Wales. Group practices are systems that incorporate the wide use of consultation and encourage a greater emphasis on ambulatory care. If these elements lead to improved public health and in turn to a decrease in need for hospitalization and decreased need for surgery, then we may expect a steady growth of group practice and of prepaid medical plans in this country. This will probably be boosted along by the growing power of large labor unions such as the Teamster's Union and the United Mine Workers. These forces appear to have been particularly effective in forcing standardization of medical care, including indications for surgery and qualifications of physicians undertaking surgery.[8,9]

A final corrective force is the growth and maturation of surgery itself as a specialty, and the influence of the surgical specialty boards with a parallel decline of general practitioners as part-time surgeons. The boards have provided exemplary leadership in the establishment of standards of practice.

L.H.N.

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Some Consequences Of Chemical And Biological Warfare

The latest contribution of the World Health Organization to the debate about chemical and biological weapons is extremely alarming.[1] The document contains a catalogue of the properties of some hitherto obscure agents. But its most alarming section contains a detailed calculation of the potential effects of chemical and biological agents directed at hypothetical targets, most densely populated cities. The document is a product of the work of the 18 member advisory committee which drafted the WHO advice to the UN later embodied in the UN report on the subject published last year.

One of the most vivid of the examples of the effects of chemical and biological weapons assumes that the agent would be the bacterium responsible for tularemia. Human beings do not often come in contact with the insect vectors of disease. It is known that as few as 25 bacterial cells can cause infection. The report points out than even the susceptibility of the bacterium to antibiotics such as streptomycin need not prevent its use as an incapacitating agent. However, a death rate of about 25 percent among infected people would otherwise be expected. Bacillus tularemia is easily grown, infection is easy by several routes, and immunization in advance is unlikely to be effective. One consequence of the use of such an agent would probably be the establishment of pools of infection among wild animals.

An attack with tularemia bacteria on a city of 5 million, would, the report estimates, produce 250,000 infected cases and probably many more. Even though most of the affected would be treated by antibiotics within 48 hours, about 25,000 would need to be hospitalized and perhaps 2,500 would die. The greatest casualties, however, would be expected among those escaping treatment early or possibly by fleeing the city. The Committee estimates that between 7-16 percent or possible 2000 additional people would die from this source making a total death rate of 4500 spread over 10 days.

If we assume that a modern city with a population of 5 million is likely to include 10,000 doctors and 60,000 nurses, the report concludes that it would probably be possible for existing medical staffs to handle the consequences of the attack at least as long as panic and severe disorganization could be avoided. This case study shows how much more resistant to an attack would be a well provided city than a city of the same size in a developing country. Thus the calculation 30,000 deaths within 10 days would be expected.

The use of plague as an infecting agent could be expected to be more damaging. It is estimated that in a city of 5 million there would probably be 150,000 cases infected with pneumonic plague, up to 100,000 hospital cases of whom 36,000 would die. One of the most serious causes of death would be secondary infection responsible for an estimated 100,000 deaths, the report says. Burial facilities would be severely taxed and untold difficulties would be expected in the cities of the same size, but without medical services for providing those initially infected without antibiotics and without hospitals on a modern scale. The report estimates that 250,000 would die on the first and succeeding waves of infection.

Nerve gas could be as damaging as pneumonic plague but act much faster. The WHO report estimates that if 150,000 people were exposed to a lethal concentration of nerve gas UX, 80,000 of them would die before help arrived and that a further 40,000 would die before help could be expected. One of the particular hazards of UX is that it is persistent and this would play havoc with the helpers. The fact that most of the deaths would be concentrated in the first 2 days would only aggravate the strain on the hospitals and medical facilities.

The panel responsible for the WHO report has also calculated the likely consequences of attempts to infect public drinking water systems with various organisms. One kilogram of freeze dried typhoid containing more than 10^{14} organisms is assumed to lose all but 5 per cent of its effectiveness on being introduced into the public water system of a city. In a modern city approximately 35,000 people would receive a sufficient high dose to be assured of developing typhoid. In less advanced cities the same amount of freeze dried bacilli would cause 130,000 cases and over 4,500 deaths.

The report goes on to analyze the consequences of the use of type A botulin toxin. Here the consequences are less certain. Because the first effects are likely to appear within 6-8 hours of infection, much will depend on how quickly public authorities will recognize what happened. It would be responsible, however, to conclude that .24 kg of toxin would cause 30,000 deaths following a 6 fold safety factor to account for unequal distribution.

In the light of such alarming consequences of chemical and biological warfare it is comforting that President Nixon announced last November that the United States would never be the first to use lethal or incapacitating chemical weapons and would never resort to biological weapons. A few days ago he also ruled out the use of toxins in warfare. The ultimate aim is, of course, to rule out War and direct our energies to the urgent tasks of peace and reconstruction.

L.H.N.

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Foreword

Today is certainly an era of revolutionary upheaval. Social and moral standards are undergoing radical changes. This is most dramatically seen in the so-called sex revolution in colleges and the extensive use of drugs. Unfortunately, occasionally this excessive drug use has a disconcerting way of backfiring, in the form of a lethal overdose or severe infection. Infective endocarditis is one of the most serious infectious disease complications of drug abuse with often the responsible pathogen being an uncommon organism. The story and death of a narcotic addict with a fungal endocarditis is exceedingly well told by Dr. Andriole in this issue.

Dramatic changes in medicine over the past half century are familiar to everyone. Initially, the aims of the medical profession were mainly palliative and diagnostic. Today, medicine seeks not only the cure but also the prevention of disease. The manuscripts submitted by Drs. Lepow and Goldschneider represent this latest approach in the prevention of viral and bacterial disease with vaccines.

When an infectious agent is isolated from a site which is normally devoid of microorganisms as the cerebral spinal fluid, its pathogenic role is easily established and must be treated. Many parts of the body have, however, a "normal flora" as the respiratory, gastrointestinal, or genito-urinary tracks. As a result, the recovery of a micro-organism from these areas does not necessarily indicate infection. Sputum cultures are one of the most notorious places where the problem is not the detection of a pathogen but rather the determination which one of the many microorganisms found is responsible for the patient's infection. Dr. Bartlett has reviewed this problem in the evaluation of sputum cultures and has shown how difficult such a task can be even with the application of quantitative sputum cultures.

Another dramatic change in recent years has been the increasing appearance of gram-negative infections in hospitalized patients. Meningitis from gram-negative organisms often constitutes a difficult therapeutic problem since the antibiotic of choice may not penetrate the blood-brain barrier adequately requiring the additional administration of the drug by the intrathecal or intraventricular route to obtain complete eradication of the infection. Information on the proper use of antibiotics by the intrathecal and intraventricular routes is relatively inadequate but I have attempted to review the current data on this subject to serve as a possible guideline for the practicing physician.

The role of adrenal corticosteroids in the management of severe meningitis is still uncertain and always induces lively debate. Dr. Thornton has discussed with unusual insight the problems that encompass this modality of therapy based to a large extent on his own excellent studies in that area.

Finally, Dr. Lewis presents a logical and prudent approach to the patients with a urinary tract infection by employing old remedies with better understanding and suggesting new therapies in appropriate situations.

RICHARD QUINTILIANI, M.D., *Guest Editor*

The Intrathecal and Intraventricular Administration of Antibiotics in Central Nervous System Infections

Richard Quintiliani, M.D.

Experimental and clinical information on the intrathecal and intraventricular administration of antibiotics is inadequate and has not kept pace with the frequent introduction of new antimicrobial agents. Many articles describe the increased occurrence of infections from gram-negative bacteria and "opportunistic" organisms in hospitalized patients.[1] This development has occurred from the greater number of patients treated with agents that impair host defenses such as multiple antibiotics, corticosteroids, immunosuppressives, and radiation. Indwelling Foley catheters, polyethylene venous catheters, tracheostomy, and mechanical ventilators often serve as the portal of entry for these micro-organisms. The increasing use of prosthetic devices as artificial heart valves or grafts serve commonly as the sites where these organisms become established and produce severe infection once they have gained entrance into the body. These organisms recovered are often sensitive only to antibiotics as kanamycin, cephalothin, or polymyxin which may penetrate variably or incompletely into the cerebrospinal fluid after systemic administration. This situation often requires their administration directly into the cerebrospinal fluid to achieve adequate bactericidal levels. This communication presents some of the available information on the use of various antibiotics by the intrathecal and intraventricular route to serve as a possible guideline for the practicing physician. It will become apparent at the end of this paper that there is inadequate information on many of these antibiotics with respect to their proper mode of administration into the spinal fluid. The need for additional information on the appropriate uses of antibiotics by this route is stressed in order that specific recommendations for their proper use can be established.

A decision to use and the dosage to administer intrathecal and/or intraventricular antibiotics should be based on the following factors:

(1) *Ability of the antibiotic to penetrate the blood-brain barrier in the presence or absence of inflammation of the meninges.*

(2) *The volume of the cerebrospinal fluid.* When making a decision of the dosage of an antibiotic to be used, it is probably more important to be familiar with the volume of the cerebrospinal fluid than the patient's body weight. In adults and children, the average volume of the cerebrospinal fluid is approximately 200 ml and 100 ml, respectively.[2] However, in the presence of hydrocephalus, the volume of the cerebrospinal fluid in children may greatly exceed that in an adult resulting in an increased dilution of the antibiotic.

(3) *The presence of an artificial drainage system (e.g. ventriculoatrial shunt) in the ventricles of the brain.* These shunts may divert antibiotics instilled into the ventricles to the blood stream making it more difficult to maintain adequate cerebrospinal fluid levels. It must also be remembered that eradication of an infection on a prosthetic device usually requires its removal along with adequate spinal fluid levels of antibiotics. Practical experience and cerebrospinal fluid assays of various antibiotics including chloramphenicol have shown that systemic antibiotics cannot be relied upon in treatment of hydrocephalic patients with ventriculitis and that it is essential to administer these antibiotics directly into spinal fluid. Generally speaking, intraventricular injections can be done fairly easily in hydrocephalus by direct injection into dilated lateral ventricules through the anterior fontanelle.

(4) *The sensitivity of the pathogen to antibiotics.* Therapeutic failures may be the result of inadequate intrathecal or intraventricular concentrations of the antibiotic. This phenomenon may occur especially in gram negative infections as *Klebsiella pneumoniae, Escherichia coli,* or *Pseudomonas aeru-*

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ginosa where relatively high minimal inhibitory concentrations of antibiotics are required to eradicate the infection.

(5) *Risk of complications of intrathecal or intraventricular antibiotics.* Convulsions, medullary coning, coma, and subdural effusion may occur as a toxic reaction to antibiotics administered directly into the neuroaxis. The risk of these complications must be weighed against the possible therapeutic advantage of administering the antibiotic directly into the cerebrospinal fluid. It is felt that an antibiotic given directly into the cisterna or ventricles may be more likely to produce a toxic neurologic reaction than if it is placed into the lumbar sac. Antimicrobial agents instilled into the lumbar spinal fluid become significantly diluted before they reach the cerebral cortex by retrograde flow. Theoretically, antibiotics injected directly into the cisterna or ventricles bypass this dilution phase and may, therefore, come into contact with the cerebral tissue in a higher concentration. As a result, it is sometimes recommended that intraventricular and cisterna injections of anibiotics be given at a dose one half the recommended intrathecal dose. However, this generalization may lead to inadequate intraventricular therapy since, as mentioned above, in many cases where intraventricular antibiotics are needed the patient has hydrocephalus where not only the volume of the cerebrospinal fluid is usually increased but also a shunting apparatus is customarily present which rapidly removes the antibiotic out from the ventricular system.

Polymyxin

Parenteral polymyxin B has an extremely poor penetration into the central nervous system. In dog experiments Schoenbach detected no antibiotic in the spinal fluid after the administration of intravenous polymyxin B at a dosage of 0.25 mg/kg/min; on the other hand, the intrathecal injection of 1 mg polymyxin B into the lumbar sac and 5 mg into the cervical cistern produced spinal fluid levels of 10 ug/ml in 45 minutes and 500 ug/ml in 45 minutes, respectively.[3] It is apparent that for effective treatment of infection within the central nervous system, polymyxin B must be given intrathecally, intraventricularly, or directly into a brain abscess cavity. Polymyxin B has been given commonly by the parenteral and intrathecal routes in the treatment of purulent meningitis caused by *Pseudomonas aeruginosa*.[4] Infants and adults given intrathecal polymyxin B have occasionally exhibited neurologic sequelae such as hypotonia of the legs, urinary incontinence or retention, convulsion and coma.[5,6] Teng and Johnson showed that the severity of the reaction to the intracisternal administration of polymyxin in dogs was dose related; 5 mg of polymyxin B given by this route gave no abnormal neurologic signs, 10 mg produced ataxia, and 50 mg resulted in death of all animals.[7] Degenerative changes of the anterior horn cells and nerve roots of the spinal cord were noted in those dogs which had received 10 mg of intracisternal polymyxin B. Clark et al performed a similar study of the toxicity of intracisternal polymyxin B in the Rhesus monkey.[8] They found that the intracisternal administration of 0.5, 1.0 and 1.5 mg of this antibiotic resulted in a mortality of 50%, 50% and 89%, respectively. It was felt that on the basis of calculated concentrations of polymyxin B in mg/ml of cerebrospinal fluid that the human clinical doses of 5, 10, and 15 mg would be comparable to the 0.5, 1.0 and 1.5 mg used in this experiment. However, similar high toxicity reactions after intrathecal administration of polymyxin B in man has not been observed. The 5 mg daily dose of intrathecal polymyxin B has been used frequently in pseudomonal meningitis in man with no fatalities from this dose reported in the literature. From information of this type, the customary recommended dose of intrathecal polymyxin B has been 2 mg every day for children under two and, for children over two and adults, 5 mg every day for 3 to 4 days and then 5 mg every other day for at least 2 weeks after sterile cerebrospinal fluid cultures.[9]

There is, however, almost no clinical information and only few experimental observations regarding the correct dosage and potential toxicity of this antibiotic when it is given by the intraventricular route. In an experiment with cats Teng found that the intraventricular and intracerebral injection of 2.5 mg and 5 mg of polymyxin B produced no clinical evidence of toxic reaction except in one animal in whom the antibiotic was injected into the left thalamus, internal capsule, and region of the hypothalamus.[10] Pathologic examination showed some inflammatory changes in the leptomeninges and minimal hemorrhage along with some softening and gliosis in the area of the intracerebral instillation of the antibiotic. Polymyxin B appears, therefore, to be somewhat toxic to the tissues of the central nervous system on direct application but, at the dosage used, no significant clinical side effects appeared.

I have personal experience with a four and a half year old hydrocephalic child who received a total of 214 mg of polymyxin B, 110 mg intraventricularly and 104 mg intrathecally during a three month hospital stay for *Klebsiella pneumoniae* meningoventriculitis. The child tolerated this medication extremely well without exhibiting any neurological complications. In addition, at no time during his therapy was there any evidence of renal impairment or respiratory difficulties as has been described with parenteral or intraperitoneal polymyxin B.[11] It must be remembered, however, that the volume of cerebrospinal fluid in patients with hydrocephalus may exceed that of a normal adult resulting in increased dilution of the antibiotic.[12] It is possible that a similar amount of polymyxin B given into a normal sized ventricular system could produce a serious toxic reaction.

Cephalothin

Cephalothin is often an effective antibiotic in many types of infections but it appears to have relatively poor entrance into the cerebrospinal fluid. Vianna and Kaye[13] showed that in humans without meningitis no detectable levels of antibiotics were achieved after intravenous administration, but in patients with meningitis levels of 0.16 to 0.31 mcg/ml were achieved. There have been a few reports of patients with bacterial meningitis treated with cephalothin in whom cerebrospinal fluid concentration varied from 0.4 to 20.7 ug/ml.[14, 15] After the rapid intravenous infusion of 2 to 4 grams of cephalothin in 14 patients either as single dose or at four to six hour intervals for several days, and in one case, for three weeks, Lerner found cerebrospinal cephalothin levels of 0.155 to 5.0 ug/ml only in those patients with cerebrospinal fluid protein content in excess of 50 mg/100 ml.[16] When the protein concentration was less than 50 mg/100 ml, no measurable drug activity could be found in cerebrospinal fluid despite serum cephalothin levels ranging up to 9.8 ug/ml. These human studies suggest that therapeutic levels of cephalothin inhibitory for most strains of staphylococci and pneumococci can be achieved in the cerebrospinal fluid in the presence of meningeal inflammation and, hence, this antibiotic may be useful in treatment of meningitis with these organisms in a patient with penicillin hypersensitivity. The scant reports with the administration of cephalothin in cases of meningococcal meningitis have been disappointing. Brown et al treated 12 patients with meningococcal meningitis with intravenous cephalothin at a dosage of 100-200 mg/kg/day.[17] Clinical results were variable with the authors coming to the conclusion that this antibiotic could not be recommended as an effective alternative to benzyl penicillin or ampicillin. Poor therapeutic results may also be expected in gram negative organisms such as *Klebsiella pneumoniae, Escherichia coli* or Proteus, where higher antibiotic levels are usually required to result in eradication of the infection. Consequently, it would be extremely useful to know the proper mode of administration of cephalothin by the intrathecal route, but extremely little data is available to make an accurate determination. O'Brien and McLaughlin administered 25 mg of cephalothin intracisternally to 11 dogs.[18] Two of the 11 animals experienced single seizures but recovered without any sequellae. A similar amount of cephalothin given to 10 dogs by the intraventricular route produced multiple seizures and death in one animal.

Until more clinical data is obtained, specific recommendations for the exact amount of cephalothin to be used intrathecally cannot be made. However, on an experimental basis, cephalothin might be given by injecting intrathecally 1 ml of a one percent solution (i.e. 10 mg/ml) in an adult with an estimated spinal fluid volume of 200 cc.; this would provide approximately 50 mcg of Keflin per milliliter of spinal fluid after diffusion and mixing of the drug. In a child with an estimated spinal fluid volume of 100 cc, this would provide 100 mcg/ml of the antibiotic. However, calculation of this type may be unreliable since they assume uniform distribution of the antibiotic and fail to take into account the possibility of its transport from the cerebrospinal fluid.

Cephloridine

Cephloridine has been used intrathecally in treating pyogenic meningitis with doses of 12.5 mg for infants, 25 mg for children aged 1 to 10 years and 50 mg for adults without any apparent side effects.[19] Cephloridine concentrations in the cerebrospinal fluid of rabbits with experimental meningitis were reasonably high with mean levels of 2.50 ± 0.32 ug/ml obtained after single intravenous administration of 12 mg/kg of the drug.[20] Walker and Collins treated 3 infants with *Hemophilus influenza* meningitis with cephloridine in dosages varying from 100 mg/kg/day to 600 mg/kg/day.[21] High cerebrospinal fluid levels were obtained only with the administration of intravenous dosages at 400 mg/kg/day (CSF levels 13.6 ug/ml to 42 ug/ml) and 600 mg/kg/day (CSF level 93 ug/ml to 104 ug/ml). Despite achievement of cerebrospinal fluid concentrations considerably in excess of those required to inhibit the pathogen, clinical deterioration and continued isolation of the organism occurred. The number of patients treated for meningitis with cephloridine is too small to decide if it is a useful alternative to penicillin.

Kanamycin

Information on the proper usage of kanamycin by the intraventricular and intrathecal routes is also inadequate. The spinal fluid levels of kanamycin after systemic administration are variable. Eichenwald found reasonably adequate levels in the spinal fluid in 8 infants without infectious disease problems and in 6 infants with bacterial meningitis.[22] After a single dose of intramuscular kanamycin (7.5 mg/kg) which gave peak serum levels of approximately 17 ug/ml, the concentrations in the spinal fluid ranged from 1/10 to 1/5 of peak serum levels in the normal infants and almost twice these concentrations were obtained in the patients with inflamed meninges. However, there is additional data which indicates that kanamycin does not achieve appreciable cerebrospinal fluid levels in the absence of meningitis. Boger and Gavin[23] and Pulaski and Tubbs[24] administered intramuscularly 1 gram and 0.5 gram kanamycin respectively to patients with uninflamed meninges and found insignificant antibiotic activity in the cerebrospinal fluid. In dogs without meningitis Tisch et al detected significant transfer of kanamycin to the cerebrospinal fluid but the amount of antibiotic given was exceedingly high (50 mg/kg IM).[25] Even in the presence of meningitis there have been some therapeutic failures despite the organism being completely susceptible to kanamycin.[26] It seems reasonable that an apparent lack of response in this type of situation indicates the possibility of inadequate transport of the drug to the spinal fluid requiring the additional administration of the antibiotic by the intrathecal route. This problem may be especially valid in newborns where organisms may not produce a good inflammatory reaction.[27] Intrathecal kanamycin has been used in the therapy of Salmonella, Klebsiella and *Escherichia coli* meninitis in dosages varying from 1 mg to 25 mg daily. Dosages in this range appear to be tolerated quite well although some of the higher amounts were given to infants with hydrocephalus again raising the possibility of increased dilution of the antibiotic. In general, the recommended dosage of intrathecal kanamycin is 1 to 5 mg daily depending on the size of the child.

Gentamicin

Gentamicin sulphate is an antibiotic which has in vitro activity against practically all the important gram negative bacteria including *Pseudomonas aeruginosa* and *Serratia marcescens.* Experience with the use of gentamicin for infection of the central nervous system is also quite limited. Preliminary information suggests that this antibiotic does not cross well into the cerebrospinal fluid and, hence, should be given intrathecally as well as intramuscularly in order to maintain adequate cerebrospinal fluid levels. Vacek et al studied the penetration of gentamicin into cerebrospinal fluid in 26 patients (ages 6 yrs. to 20 yrs.) suffering from mumps meningoencephalitis after the administration of a single intramuscular dose of 1.2 to 4.0 mg/kg.[28] They found cerebrospinal fluid drug activity in only 5 of the 26 persons with the highest level being 0.19 ug/ml. Newman and Holt treated eleven patients with gentamicin in a dosage of 1 mg daily intraventricularly and 2 mg/kg/day intramuscularly in divided doses.[29] Of the eleven cases treated, the organisms recovered were *Klebsiella pneumoniae* (6 cases), *Pseudomonas aeruginosa* (2 cases), *Escherichia coli* (2 cases) and *Proteus mirabilis* (1 case). There were three treatment failures in this group, two with pseudomonal meningitis and one with *Escherichia coli* meningitis. It is interesting that in one of the patients with pseudomonal meningitis, infection was eliminated with the use of polymyxin B and not with gentamicin. In the other patient with pseudomonal meningitis who failed to respond, the cerebrospinal fluid levels of gentamicin were well in excess of those needed to inhibit the bacteria. Leedom et al administered intrathecal and intraventricular gentamicin in a dosage of 1 mg to 4 infants between the ages of 2 weeks and 10 months.[30] In two of the patients treated in this manner, the cerebrospinal fluid cultures remained positive for the organisms (*salmonella urbana,* "paracolon") despite the administration of this antibiotic directly into the cerebrospinal fluid. In 3 hydrocephalic infants treated for *Kelbsiella pneumoniae* meningitis and ventriculitis with gentamicin at dosages of 2 mg/kg/day and 1 mg intraventricularly, cerebrospinal fluid levels from 2 to 7 ug/ml were obtained.[31] In one of the patients, the CSF level fell to zero when the intraventricular administration of the antibiotic was stopped despite continuation of parentheral therapy. The finding of no drug activity in the cerebrospinal fluid after intraventricular therapy was discontinued suggests the important role that the administration of the antibiotic by this route played in the eradication of the infection. It is of considerable interest that despite a difficult organism to eradicate, all three children were cured of their infection with the combination of intrathecal and intramuscular gentamicin. Fasano used an intraspinal dose of gentamicin of 80 mg b.i.d. for three days for control of sepsis following brain surgery in 2 patients without any apparent toxic reaction to the antibiotic.[32] In one patient Fasano administered 80 mg gentamicin every 12 hours directly into the cornu frontale of the lateral ventricle without any problems. The marked variation in the amount of intrathecal gentamicin used again demonstrates lack of adequate experience to fall back upon to make an accurate determination as to the proper dosage.

Streptomycin

Intrathecal streptomycin formerly was used commonly in the therapy of *Hemophilus influenza* meningitis. However, with the excellent therapeutic results with the administration of parenteral ampicillin for this illness, the need for the intrathecal use of streptomycin has largely been abandoned. Streptomycin, as other aminoglycoside antibiotics, does not pass readily into the cerebrospinal fluid. It is also capable of producing serious nervous system reactions when given in excessive amounts. It is imperative that great care be given to the proper dosage before instillation into the lumbar sac since the safe dosage range for intrathecally administered streptomycin is very narrow. In infants less than two years of age, no more than 25 mg should be given. This dosage may be increased to 25 to 50 mg for children and 75 mg for adults. It is also important that the antibiotic be freshly prepared from crystalline streptomycin sulphate. As with intrathecal penicillin, it should be diluated in 10 cc of physiologic saline and injected at a rate of 1 ml/min after the removal of a comparable amount of cerebrospinal fluid.[33]

Penicillin

In health, penicillin passes poorly into the cerebrospinal fluid. Under normal conditions the intravenous dosages of even 25 million units daily rarely give spinal fluid levels above 0.5 units per ml. However, when the meninges are acutely inflamed, penicillin penetrates into the cerebrospinal fluid more easily and usually achieves adequate levels in the cerebrospinal fluid to eradicate the more common forms of bacterial meningitis such as those due to *Diplococcus pneumoniae* and *Neisseria meningitides* by the intravenous route alone. There has been a tendency to avoid intrathecal penicillin if possible in view of its potent epileptogenic properties. In fact, neurotoxicity may occur from penicillin by the intravenous route alone usualy in presence of underlying nervous system disease, renal impairment or inappropriately large doses for elderly persons.[34] In early experiments by Walker et al it was shown that the application of as little as 500 units to the cerebral cortex of macaque monkies produced convulsions.[35] Neymann et al showed that the intracisternal administration of 40,000 to 100,000 units penicillin was capable of inducing seizures in patients being treated for general paresis.[36] The conventional dosage for the intrathecal administration of crystalline penicillin G has been 1000 to 5000 units for infants under the age of two, 5000 to 10,000 units for children two to ten, 10,000 to 15,000 units for children ages ten to fifteen, and 20,000 to 30,000 units for older individuals. When given in thtse dosages, the intrathecal administration of penicilin is quite safe. The main problem has been its incorrect administration either from mistakes in calculation of dosage or from too rapid administration. It is important to dilute the antibiotic in 10 cc of physiologic saline and to administer it at a rate no faster than 1 ml per minute. A comparable volume of cerebrospinal fluid is usually withdrawn prior to the instillation of the antibiotic.

Ampicillin

Parenteral ampicillin has been used commonly as the drug of choice in the unknown meningitis in children because of its well known ability to eradicate the most common pathogens involved in pediatric cases of meningitis, namely the *Diplococcus pneumoniae, Neisseria meningitides* and *Hemophilus influenza*. Since all of these organisms are inhibited by ampicillin in a concentration of less than 1 mcg per milimeter, there is usually no need for the additional administration of this antibiotic by the intraventricular or intrathecal routes. However, in the absence of meningeal inflammation or in the presence of a pathogen which requires a higher minimum inhibitory concentration of the antibiotic (for *Escherichia coli*, the minimum inhibitory concentration of ampicillin is often 2 to 4 mcg/ml) adequate levels in the spinal fluid can only be achieved with complete assurance by the direct instillation of this antibiotic into the thecal space or into the ventricles. The customary dose for intrathecal or intraventricular ampicillin is 3 to 5 mg for infants and young children, 5 to 10 mg for children over 12 years of age, and 10 to 40 mg for adults.

Bacitracin

Bacitracin is often a forgotten antibiotic today. However, one of its important uses is in the therapy of infections of the nervous system by the staphylococcus. Bacitracin can be used by either the intrathecal or intraventricular route with considerable safety in view of an extremely low tendency to be eleptogenic or to produce other problems of nervous system toxicity. Its main use has been in the neurosurgical field where the staphylococcus (usually *Staphylococcus epidermidis*) remains as the most common etiologic agents of meningitis following neurosurgical procedures. Tht usual dosage of intrathecal and intraventricular bacitracin is 500 to 1000 units in neonates, 1000 to 5000 units in children and 5000 to 10,000 units in adults.

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Endocarditis In The Drug User

Vincent T. Andriole, M.D.

It has been estimated that over 100,000 persons in the United States are addicted or habituated to opiates and many more use opiates intermittently.[1] Regardless of whether the person has acquired physical dependence on these drugs or has become a chronic or intermittent user without physical dependence, the user employs techniques of self-administration of opiates with complete disregard for the simple principles of good hygiene. Such practices of self-administration have been associated with severe medical complications which include hepatitis, tetanus, cellulitis, pulmonary infections, overdose and endocarditis.[1-6] The purpose of the present report is to focus on the last mentioned medical complication, namely endocarditis in the drug user. The following case report emphasizes a number of important features of this disease in narcotic users.

Case Report

On March of this year, a 25-year-old white male was referred to us from a near-by hospital with the following history: He had been a heroin addict for the past 8 years and had an episode of serum hepititis. In 1968, he was placed on the methadone program but began using intravenous cocaine along with the methadone. On January 27, 1969 he was admitted to a near-by hospital because of spiking fever and low back pain. On admission there, he was found to have conjunctival hemorrhages, splenomegaly, an Osler's node, and murmurs of aortic insufficiency and aortic stenosis. He was thought to have bacterial endocarditis and antibiotic treatment was instituted. However, blood cultures grew out *Candida parakrusei* on February 13, 1969, and he was begun on amphotericin B therapy intravenously on February 25, 1969. The patient became afebrile on amphotericin B and clinically improved. On March 25, 1969, he had the sudden onset of numbness and a cold sensation over the right leg. The right popliteal pulse was absent and a diagnosis of embolism to the right femoral artery was made. The patient underwent an embolectomy under local anesthesia. Cultures of the embolus grew *Candida parakrusei* in spite of the fact that he was on amphotericin B therapy. During his hospital stay his diastolic murmur increased in intensity and his blood pressure fell to levels of 140 systolic over 30 diastolic. Three days after the embolectomy was performed he was transferred to the Yale-New Haven Hospital for further evaluation and care.

When we saw him for the first time he was in acute distress with obvious signs of aortic insufficiency and with a blood pressure of 140 systolic over 20 diastolic. A systolic ejection murmur was audible along the left sternal border and a very loud diastolic blow was heard in the aortic area and down along the left sternal border. He had pistol shot sounds over the femoral vessels and obvious capillary pulsations of the nail beds. He had been on amphotericin B therapy since February 25, 1969. His blood urea nitrogen value on admission was 50 milligrams per 100 milliliters and his serum creatinine value was 3.7 milligrams per 100 milliliters. The patient had such severe aortic insufficiency that we felt his only chance for survival was to undergo aortic valve replacement. However, we were unable to continue to treat him with amphotericin B because of his compromised renal function. During the next weeks, his clinical course deteriorated but his blood urea nitrogen value fell to 18 milligrams per 100 milliliters and his serum creatinine value to 1.5 milligrams per 100 milliliters. Consequently, amphotericin B therapy was started again on April 9, 1969, and the patient underwent insertion of a Starr-Edwards aortic valve prosthesis on April 11, 1969. At surgery, the patients' aortic valve was totally destroyed and had large vegetation growing upon the remnants of the leaflets. There was also a 1 by 1 centimeter abscess in the left lateral border of the valve was totally destroyed and had large vegetations growtime of surgery, the abscess was irrigated locally with amphotericin B. Following surgery the patient continued to improve and continued to receive amphotericin B intravenously. On May 1, 1969, a recurrence of the aortic diastolic murmur was first noted while the patient was still receiving amphotericin B therapy. This suggested that he had a valve leak with continued infection at the suture line. Although blood cultures were sterile during the month of April, blood cultures on May 2, 12, 15 and 16, 1969, grew *Candida parakrusei,* even though the patient was still receiving amphotericin B intravenously. It became clear that we were not going to sterilize the prosthetic valve infection and that he would have to undergo a second valve replacement. The patient was allowed to go home and was followed closely with the intention of readmitting him for a second valve replacement and another course of amphotericin B treatment at the first signs of aortic decompensation. The patient remained home approximately one month and was readmitted on June 23, 1969, for a second aortic prosthetic valve replacement. He was restarted on amphotericin B therapy and underwent prosthetic aortic valve replacement on July 1, 1969. At the time of surgery the first prosthetic aortic value was grossly infected with vegetations over the struts and all around the sewing ring. The first prosthetic aortic valve was removed (Figures 1 and 2) and a fresh aortic valve was sutured into place.

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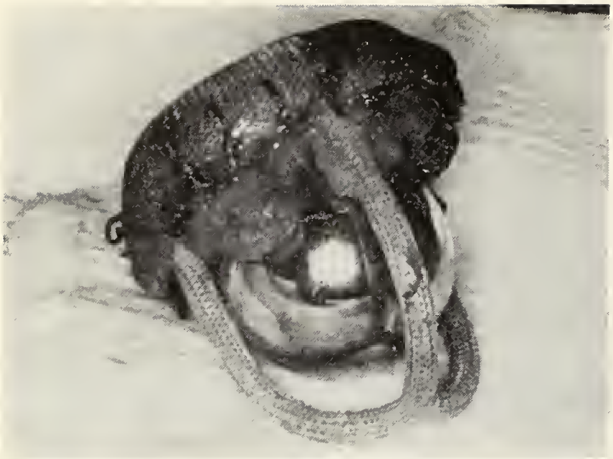

Figure 1

First prosthetic aortic valve removed because of continued infection. Large vegetations of *Candida parakrusei* around the struts and sewing ring.

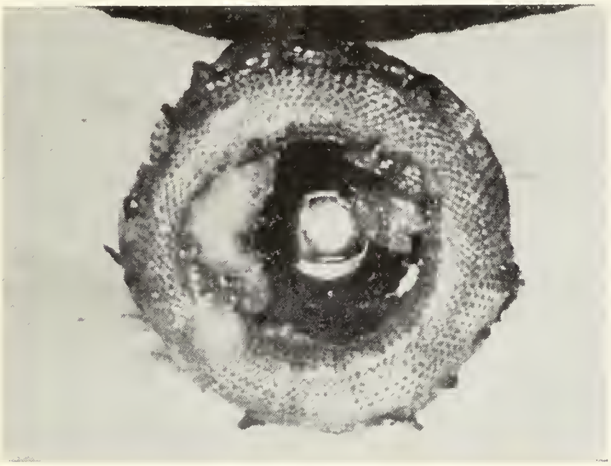

Figure 2

First prosthetic aortic valve removed because of continued infection with huge vegetations of *Candida parakrusei* protruding into orifice.

Blood cultures during the 2 weeks prior to the second operative procedure also grew *Candida parakrusei*. The patient had a very stormy post-operative course. Despite numerous supportive measures and continued intravenous amphotericin B treatment, he died on July 27, 1969. The second prosthetic aortic valve contained many vegetations which on microscopic examination contained many colonies of yeast. There were no endocardial lesions.

The medical history, physical findings, and clinical course of this patient emphasize a number of important features. First, that endocarditis in the drug user is a real problem. Second, that from a microbiologic point of view, the type of endocarditis seen in the drug user is different from that seen in the non-addict. Third, that the clinical picture of endocarditis in the drug user is also different from that seen in the non-addict and finally, that this disease in the drug user is more serious than endocarditis in the non-addict in spite of aggressive attempts to alter its course.

If we examine the first point, namely that endocarditis is a real problem in addicts one can look at this in at least two ways. For example, endocarditis accounts for 8 to 10 per cent of all the infectious complications that we have observed in addicts.[2-4, 7, 8] Furthermore, if you calculate the incidence of endocarditis in drug users and compare that to the incidence of endocarditis in non-addicts with valvular disease, the risk in the addict is three times greater than in the non-addict, even though the non-addict is predisposed because he has valvular disease.[4]

In regard to the second point, that from a microbiologic point of view, the type of endocarditis seen in the drug user is different from that seen in the non-addict. One can look at the microbiologic pattern of infectious endocarditis seen in the addict and compare it to the types of endocarditis seen in an non-addict population.

Table 1 lists the organisms responsible for endocarditis in one hundred narcotic users who developed this complication and includes our experience in addition to the observations of others.[1-6] Staphylococci were the causative organism in 47 addicts, whereas staphylococci are responsible for endocarditis in only 25 per cent of non-addict patients with this disease.[9] *Streptococcus viridans* is rarely seen in the addict, yet this organism accounts for 60 to 70 per cent of endocarditis in the non-addict population. In addition, the incidence of gram-negative infections is much higher in drug users than in non-addicts. Gram-negative infections are rarely seen in non-addicts, except in patients who have had cardiac surgery. Furthermore, the incidence of candida endocarditis in the drug user is fantastically higher than the incidence of endocarditis due to this organism in non-addict patients. These dif-

TABLE 1

ENDOCARDITIS IN NARCOTIC USERS

Organisms	*Per Cent*
Staphylococcus aureus	44
Staphylococcus albus	3
Streptococcus faecalis	13
Streptococcus viridans	4
Gram-Negatives	13
Candida	20
Unknown	3

ferences in microbial etiology can best be explained by the fact that addicts are not compulsively hygenic in their technique of self administration. In addition to injecting their particular choice of narcotic, they are probably repeatedly inoculating themselves with significant numbers of these organisms. For example, there is one drug user on record with three different episodes of endocarditis.[4]

There is one other interesting point about the type of organisms involved in endocarditis in drug users. These organisms can produce endocardial damage in the absence of pre-existing valvular abnormality. Only species of candida are generally thought to be incapable of invading normal valves. However, there are two cases of candida endocarditis which occurred in addicts with no evidence of pre-existing valvular disease. Interestingly enough, both patients were infected by *Candida parakrusei* which, in fact, is one of the less virulent species of candida. The present report describes one of these patients, and the other, we reported in 1962.[6] In general however, candida organisms are not likely to infect normal heart valves.

One way to examine the third point, that the clinical picture of endocarditis in the drug user is also different from that seen in the non-addict is to compare the valve involvement in these two groups of patients (Table 2). One finds that there is not a great deal of difference in aortic valve involvement even if you combine those cases with aortic valve involvement alone, or aortic and mitral valve infection. The latter figures are 47 per cent in the drug user as compared with 45 per cent in the non-addict.[4] There is a considerable difference in isolated mitral valve disease which is much more frequent in the non-addict patient. What is really impressive, however, is the incidence of tricuspid infection either alone or associated with infection of one of the other valves. Tricuspid endocarditis is much more frequent in the drug user (Table 2).

TABLE 2

VALVE INVOLVEMENT IN ENDOCARDITIS

Valve	*Addicts*	*Non-Addicts*
Aortic	35%	28%
Aortic and Mitral	12%	17%
Mitral	22%	48%
Tricuspid	24%	0%
Tricuspid and Other	5%	4%
Unknown	2%	4%

Furthermore, the clinical picture in the addict is one of an acute fulminating type of endocarditis with major embolic phenomenon and marked valve destruction as was demonstrated in the patient described in this report. Because of the fulminant nature of this disease in addicts, it seems imperative to suspect this diagnosis in the drug user and to institute appropriate treatment early in an attempt to prevent subsequent valve destruction. One form of this disease may pose a diagnostic problem (Table 3). That the incidence of tricuspid endocarditis in the addict is significant has already been mentioned. This diagnosis should be suspected when the patient develops the sequential appearance of discrete pulmonary lesions in different parts of the lung, (which is often referred to as embolic pneumonia). Furthermore, these patients rarely have a cardiac murmur. Since the lung does not effectively remove the bacteria, these patients may also have evidence of systemic emboli to the kidneys, brain, eyes and other organs, and blood cultures are usually positive. Although staphylococci may infect valves on either side of the heart, if the tricuspid valve is involved, the infecting organism is almost invariably the staphylococcus.

TABLE 3

TRICUSPID ENDOCARDITIS IN ADDICTS

1. Sequential appearance of discrete pulmonary lesions in different parts of lung. (Embolic pneumonia)
2. Cardiac murmur usually absent.
3. Systemic embolism
4. Positive blood cultures (staphylococci)

The final point is the seriousness of this disease in the addict. The mortality rate is high in endocarditis in drug users and approximates 70 per cent.[1] The mortality is even higher in candida infections.[6] To my knowledge, only one of the 20 patients with candida infections is still living and she is still under treatment. In contrast, patients with staphylococcal endocarditis have a better prognosis. Recovery from infection is approximately 60 per cent when the diagnosis is made antemortem.[1]

In summary, drug addicts are providing us with an awesome picture of a fulminant type of endocarditis, produced by organisms which are destructive, and fortunately, not as frequently seen in non-addict patients with endocarditis. This problem is a real one in addicts. Although the mortality is great, early diagnosis and treatment in staphylococcal endocarditis provides a reasonable chance for survival.

Nevertheless, drug addiction is an "Impossible Mission", and the patient is likely to self-destruct in "five seconds."

Acknowledgement

The technical assistance of Daria DeRose is most gratefully appreciated.

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Society To Conduct Group Practice Survey

A council-appointed Ad Hoc Committee to Study Group Practice informed the Council recently of its plans to conduct a survey of groups in Connecticut. The purpose of the survey will be to gather information about various aspects of group practice; i.e. different types, advantages to patients, advantages to member physicians, quality of care, economies in costs, etc.

The definition of a "group", in the context of the survey, is: "Three or more physicians using common office facilities, using common diagnostic facilities, and being in a professional partnership or corporation."

The Ad Hoc Committee has already compiled a listing of most of the groups operating currently in the state and these are the ones that will be surveyed by questionnaire. The questionnaire, now being drafted by the Committee, will be a modification of the AMA's "Register of Group Practice".

It is hoped that all those surveyed will respond to all questions asked in the questionnaire, and will return the completed documents promptly to the Society's headquarters office.

The members of the Ad Hoc Committee are:

James H. Root, Jr., Waterbury, Chairman
Carl W. Johnson, Thompsonville
William M. Edmonstone, Mystic
Edward Martin, New Britain
George J. Geanuracos, Bridgeport

Adrenocorticosteroid Therapy of Bacterial Meningitis

George F. Thornton, M.D.

Prior to the availability of chemotherapy, bacterial infections of the meninges were almost universally fatal. With the development of effective antimicrobial agents, survival in bacterial meningitis has improved markedly. Nevertheless, a significant number of patients succumb to infection and many survivors are left with serious neurologic sequelae.[1-4] Mortality and morbidity vary with infecting organism, age of the patient and severity of illness at the time of initial antibiotic therapy.[1-5] Inability to eradicate the infecting organism does not seem to be an important factor.[6] Persistence of significant mortality and neurologic damage despite adequate chemotherapy has suggested that additional therapeutic measures directed at aspects of bacterial meningitis not dependent on the continued presence of viable bacteria might significantly improve survival and reduce neurologic sequelae.[6]

Pyogenic Meningitis

Mortality in bacterial meningitis varies from 3 to 60%, depending on the patient's age, infecting organism and severity of illness on admission to hospital.[1-5] Mechanical factors within the cranial vault appear to be significant in most early pyogenic meningitis deaths.[7, 8] Autopsy studies of patients dying of acute meningococcal meningitis may show nothing more than acute cerebral edema.[8] At postmortem examination *Hemophilus influenzae* meningitis is associated with basilar inflammation, cerebral edema and occasionally arteritis and phlebitis.[8] Pneumococcal meningitis is characterized by cerebral edema and is often associated with vascular invasion leading to secondary cortical infarction.[7, 8] In addition, a significant number of patients with overwhelming septicemia and meningitis die suddenly early in the disease in peripheral vascular collapse often, but not invariably associated with bilateral adrenocortical hemorrhage.[5, 7, 8]

Neurosurgical decompression and osmotic diuretics have all been suggested as possible adjuncts to the antibiotic therapy of pyogenic meningitis.[6] Adrenocorticosteroids have also been suggested as reasonable supportive therapy in acute bacterial meningitis.[6] Experimentally, steroids are capable of reducing the intensity of the inflammatory response, reducing cerebral edema and may have a beneficial effect on the cardiovascular response to sepsis.[9]

Isolated case reports and small, uncontrolled series have suggested that adrenocorticosteroids may significantly alter the outcome in acute bacterial meningitis.[6, 10] However, five controlled studies have shown no significant benefit attendant with the use of steroids in either high or low doses (Table 1). Lepper and Spies studied 129 patients with bacterial meningitis predominantly in the pediatric age group.[11] Twenty-three of the patients had pneumococcal infections, 57 were infected with *H. influenzae* and 49 with meningicocci. All patients were treated with an appropriate antimicrobial (not standardized). Mortality was low (2 deaths) and was not significantly different in either treatment group. There was suggestive evidence of an adverse effect in the clinical course of *Hemophilus influenzae* meningitis in the steroid-treated group. The study was not "double-blind" and involved patients receiving various antimicrobial agents in a concurrent chemotherapy study. These deficiencies in experimental design weaken the conclusions drawn.

Patients with bacterial infections of the central nervous system constituted the largest group in the Cooperative Study of the use of adrenocorticosteroids in overwhelming sepsis (85 of 194 patients) (Table 1).[12] Patients included in the study were predominantly adults and were hospitalized at five different cooperating institutions throughout the United States. They were assigned randomly to a steroid-treated or control group receiving placebo. The study was double-blind and included 56 patients with pneumococcal meningitis in the older age group. Mortality was high in both steroid and control groups. There was no detectable benefit

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TABLE 1

SUMMARY, CONTROLLED STUDIES, CORTICOSTEROID THERAPY, PYOGENIC MENINGITIS

					Mortality	
Study	Double-Blind	Steroid Dose	Bacteriology	No. Patients	Steroid-treated	Control
					(Deaths/Total Patients)	
Lepper & Spies (11)	No	Hydrocortisone 250mg qd × 5 ACTH qd × 2 (Adult)	*H. influenzae*	57	0/28	0/29
		2.5mg/Kg qd × 5	*N. meningitidis*	49	0/22	0/27
		ACTH qd × 2 (pediatric)	*D. pneumoniae ?*	23	1/11	1/12
Cooperative Study Group (12)	Yes	Hydrocortisone 300mg ↓ over 6 days	*D. pneumoniae ?*	56	12/26	15/30
			N. meningitidis	9	1/4	2/5
			Unknown	10	2/4	2/6
			M. tuberculosis	6	1/2	3/4
Thornton, et al (13, 14)	Yes	Methylprednisolone 125 mg q6h × 8 followed by 125mg q12h × 4	*D. pneumoniae*	37	9/19	9/18
			N. meningitidis	22	0/14	1/8
			H. influenzae	9	3/5	2/4
			Unknown	18	1/7	1/11
deLemos & Haggerty (3)	Yes	Methylprednisolone 40 mg q6h × 12	*H. influenzae*	69	1/32	0/37
			N. meningitidis	16	0/9	0/7
			D. pneumoniae	13	1/5	1/8
			Unknown	16	0/6	0/10
Belsey, et al (4)	Yes	Dexamethasone 1.2mg/M^2 q6h × 16	*H. influenzae*	54	2/43	1/43
			N. meningitidis	22		
			D. pneumoniae	6		
			Unknown	4		

from steroid administration. The comparability of host factors and antibiotic therapy is not reported.

We have recently reported the results of a controlled, double-blind study of high dose steroid therapy in pneumococcal meningitis.[13] In addition, a large number of patients with meningococcal meningitis, *Hemophilus influenzae* meningitis and pyogenic meningitis, cultures sterile, were also studies in a similar fashion.[14] For the first time an attempt was made to match patients by suspected etiologic agent, age and presence or absence of coma on admission to hospital. Patients received 500 mg of methylprednisolone (equivalent to 2 grams hydrocortisone) daily for two days followed by 250 mg daily for two additional days. Mortality was high in this predominantly adult population. There was no significant difference in mortality in either steroid-treated or control patients (Table 1). Serious neurologic residua were seen predominantly in patients with pneumococcal meningitis. There was no difference in the incidence of sequelae in either the steroid-treated or control group. The rate of return to normal values of CSF cell-count, sugar and protein was not significantly affected by steroid therapy. Although mortality and neurologic complications were identical in steroid-treated and control patients, the duration of hospitalization in the steroid-treated and control patients dying of pneumococcal meningitis was strikingly different. Seven control patients dying of pneumococcal meningitis survived a mean of 30 hours with a range of 2 to 110 hours while the steroid-treated patients with fatal pneumococcal meningitis were hospitalized for a mean of 176 hours with a range of 6 to 570 hours. Steroid-treated patients tended to survive the fulminant initial course of the disease only to succumb days to weeks later of secondary complicating problems developing in severely brain-damaged patients. These striking results suggest that massive adrenocorticosteroid therapy was of benefit in controlling cerebral edema and the toxemia of pneumococcal infection but could not prevent neural injury.

deLemos and Haggerty have recently reported their experience with methylprednisolone in 109 pediatric patients (neonatal meningitis excluded) (Table 1).[3] Patients were randomly assigned to steroid (40 mg methylprednisolone) or placebo without attempts to match by age, etiologic agent or severity of illness. *Hemophilus influenzae* meningitis constituted the largest group (69 patients). 16 patients had meningococcal meningitis, 13 pneumococcal, 3 unusual bacterial species and in 16, the responsible agent was not identified. Mortality was quite low (2 deaths in the steroid-treated group; 1 death in the control) and was not significantly different in the two groups. Serious neurologic sequelae were more frequently detected in the steroid-treated patients than in controls, giving further support to the concept that steroid therapy is unable to prevent neural injury in bacterial meningitis.

Belsey, Hoffpauir and Smith have reported results of a double-blind study of dexamethasone as an adjunct to the therapy of acute bacterial meningitis (Table 1).[4] Their study is also well-designed and attempts to match patients by age, etiologic agent and mental status on admission. 102 pediatric patients were included. Patients were treated with dexamethasone, (1.2 mg/M^{2}q6h x 16 doses), or placebo. In 58 instances, *Hemophilus influenzae* were recovered while meningococci were responsible for 27 cases, pneumococci for 8 and in 9, cultures were sterile. Only three deaths were recorded. Analysis of 86 matched pairs showed no significant difference in mortality. Eight patients in the dexamethasone group developed significant complications while 18 placebo patients developed complications. These differences, although statistically significant, could not be clearly related to the effectiveness of steroid therapy. It was the conclusion of the authors that there is no demonstrable difference in mortality or morbidity between steroid-treated and control patients.

Tuberculous Meningitis

The prognosis in tuberculous meningitis has improved significantly with the use of isoniazid (INH) and streptomycin.[15] Nevertheless, significant mortality and morbidity are still encountered in advanced and moderately advanced disease.[15] There is considerable evidence that hypersensitivity to tuberculin protein is a significant factor in the pathogenesis of this disease.[15] Experimentally, adrenocorticosteroids have been shown to suppress the inflammatory response and have been proposed as adjuncts to the chemotherapy of tuberculosis whenever suppression of inflammation as well as eradication of the tubercle bacillus is desirable.[16] Uncontrolled studies and isolated case reports suggest that steroid therapy has a beneficial effect on the course and outcome of tuberculous meningitis.[17, 18]

There are only two controlled, published studies designed to evaluate the benefits of corticosteroid therapy in tuberculous meningitis (Table 2).

Lepper and Spies using alternate case randomization, were unable to demonstrate benefits in either mortality or morbidity in 18 steroid treated patients when compared with 19 controls (Table 2).[19] No attempt at matching patients by severity of illness was attempted and it is not clear if the steroid-treated and control groups were entirely comparable. In addition, two weeks may not be sufficiently long to demonstrate any beneficial steroid effect.

We have recently reported our experience in a double-blind study of 23 patients with tuberculous meningitis treated with dexamethasone (Table 2).[15] An attempt to match patients by severity of illness and age was included in the experimental design. Although mortality was lower in the steroid-treated group (6 out of 11 patients) when compared with controls (9 out of 12 patients), the results were not significant statistically. A striking steroid effect was observed on CSF values suggesting that the intrathecal tuberculin reaction can be suppressed with steroid therapy. In addition, steroids seem to control cerebral edema and the frequency of cen-

TABLE 2

SUMMARY, CONTROLLED STUDIES, CORTICOSTEROID THERAPY, TUBERCULOUS MENINGITIS

Study	Steroid Dose	No. Patients	Mortality Steroid-treated	Control
			(Deaths/Total Patients)	
Lepper & Spies (19)	Hydrocortisone 4mg/Kg/day × 14 days ACTH 0.5u/Kg/day Day 11-14	37	7/18	6/19
O'Toole, et al (15)	Dexamethasone 9mg qd tapered over 4 weeks (Adult)	23	6/11	9/12

tral herniation early in the course of the disease. These findings strongly suggest that steroid therapy may be beneficial in the initial management of tuberculous meningitis.

Summary

Mortality and morbidity of pyogenic meningitis is related predominantly to the patients' age, severity of disease on admission to hospital and etiologic agent. There is no convincing evidence that adrenocorticosteroid therapy is of benefit as an adjunct to the antibiotic management of patients with pyogenic meningitis. Severely toxemic adult patients with pneumococcal meningitis may be protected from cerebral edema and the hemodynamic effect of overwhelming sepsis but steroids do not seem to prevent neural injury or subsequent death.

Steroid therapy of tuberculous meningitis does seem indicated in that adrenocorticoids are capable of suppressing the inflammatory reaction in tuberculous infection of the meninges. It remains to be demonstrated that suppression of the meningeal reaction is associated with a better prognosis.

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Vaccination Against Meningococcal Meningitis

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The Problem:

Since it was first identified as a discrete clinical entity in 1887, meningococcal meningitis has occurred sporadically or in epidemic form throughout temperate and tropical areas of the world. In the United States, more than 95% of cases of meningococcal meningitis have been caused by organisms belonging to serogroups A, B, and C.[1] Group A meningococci have been responsible for all epidemics in the civilian population. These organisms had not been seen in this country for approximately 15 years, but recently several clinical cases of group A meningitis were confirmed by the National Communicable Disease Center, Atlanta, Georgia. This is of considerable concern, inasmuch as epidemiological data suggests that a nationwide epidemic is overdue (Fig. 1). Groups B and C meningococci have caused sporadic cases of meningitis during inter-epidemic periods. However, the potential for major outbreaks of group B and C meningitis was demonstrated at several military bases during the past few years.

Meningococcal meningitis is a particularly serious problem among children. Of the 3,000 to 4,000 cases that are reported in the United States each year, and the 30,000 to 80,000 cases that occur every 10 to 15 years during epidemics, more than 50% occur in children under the age of 5 years (Fig. 2). Despite the effectiveness of penicillin in the treatment of systemic meningococcal disease, the mortality in the civilian population fluctuates between 25 and 30%, and is even higher in the pediatric age group. This is due to several factors, among which are difficulties of early diagnosis and frequency of fulminant course in young children. The disease is particularly lethal among children under 2 years, and severe neurological sequellae are frequent among survivors.

During periods of mobilization, meningococcal meningitis is a problem among military recruits. As an example, at Fort Dix, New Jersey, in winter 1968 the attack rate of meningococcal disease was approximately 1 per 200 recruits per 4 weeks basic training. This was 300 times the concurrent incidence in the civilian population. Outbreaks of meningococcal meningitis have also been reported in other closed populations, such as boarding schools, nursing homes and custodial institutions.

Prophylaxis Against Meningococcal Disease:

For more than 20 years sulfadiazine had been a model prophylactic agent against systemic meningococcal disease. When used in closed populations, small amounts of sulfonamides suppressed disease by eradicating meningococci from the nasopharynx of asymptomatic carriers, the reservoir for most meningococcal illness. However, over the last 6 years emergence of sulfonamide-resistant strains of

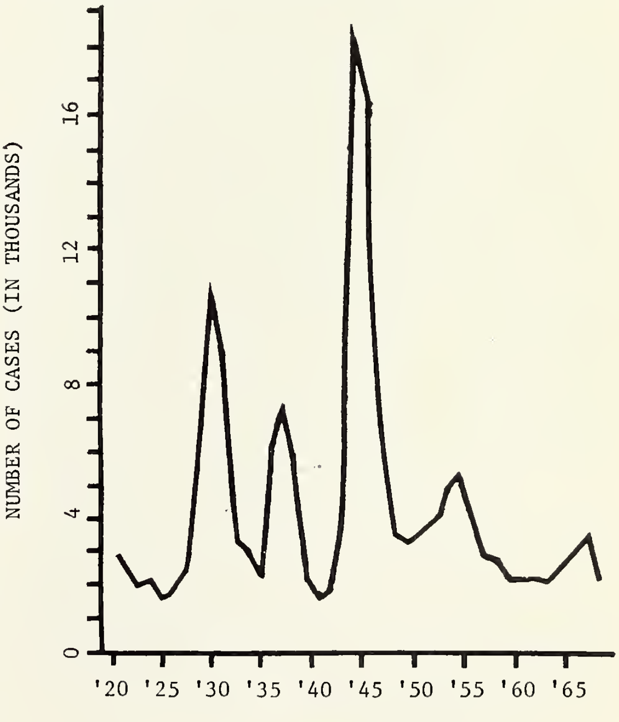

Figure 1

Reported cases of meningococcal disease in the United States, 1920-1967.

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meningococci of serogroups A, B and C has created an acute situation with respect to prevention of meningococcal disease. Meningococci resistant to sulfadiazine at concentrations of 1μg per ml (0.1 milligram %) are now the rule. With the exception of a recent report using Rifampin,[2] attempts at prophylaxis using other agents have been unsuccessful. In extensive studies among military recruits, no other chemotherapeutic drug has proved capable of preventing or eliminating the meningococcal carrier state under field conditions.

Because of the fulminant course of many cases of meningococcal meningitis, particularly among children, reliance upon therapeutic measures for control of meningococcal disease is not sufficient. Clearly, long-lasting prophylactic measures are needed. The present report summarizes research done at the Walter Reed Army Institute of Research, Washington, D.C. towards the development of vaccines against systematic meningococcal disease.[3-9] This work was done in collaboration with Emil C. Gotschlich, currently Associate Professor at the Rockefeller University, and Malcolm S. Artenstein, Director of the Department of Bacterial Diseases at Walter Reed.

Past Experiences with Meningococcal Vaccines:

More than a score of large scale attempts have been made to develop a vaccine to combat meningococcal meningitis.[10] Several of the vaccines were clearly ineffective, while others yielded inconclusive results. A vaccine prepared at the Pasteur Institute in Brazzaville from 1936 to 1939 was apparently successful. Unfortunately, the material produced by the same institute after World War II was no longer effective. Inasmuch as all these vaccines consisted of killed meningococci or crude extracts from meningococcal cultures, it is understandable that results varied greatly from batch to batch. Furthermore, severe local and systemic reactions, presumably due to endotoxin, were frequently observed.

During the mid-40's studies by several investigators[11,12] indicated that antibodies to the group-specific meningococcal polysaccharides were able to passively protect mice against experimentally induced infection. However, attempts to immunize human volunteers with purified group A and C meningococcal polysaccharides were unsuccessful.[13] Such purified polysaccharides appeared to be non-antigenic in man.

Recent Developments:

Two developments at Walter Reed reawakened interest in the possibility that group-specific meningococcal cell wall polysaccharides could be used as vaccines against systemic meningococcal disease. The first was the finding that circulating antibodies in normal individuals play a major role in defending against *naturally* occurring meningococcal disease;[3] and that the bulk of such protective antibodies are directed against the group-specific polysaccharides.[4] The second was the development of a method for the isolation of group specific meningococcal polysaccharides in large molecular weight form (i.e. MW greater than 100,000).[5] Experiments by others with graded dextrams[14] had shown that antigenicity of polysaccharides in man was a function of their molecular weights (the higher the more antigenic). This suggested that highly polymerized meningococcal polysaccharides also might be antigenic in man.

Natural Immunity to Meningococcal Meningitis:

Over the years, epidemiological observations on incidence of meningitis, immune response to systemic infection, and therapeutic effects of passively transferred hyperimmune serum have suggested that humoral antibodies are important in defense against meningococcal disease in man. In our studies it was found that the age related incidence of meningococcal meningitis in the general population was inversely related to the prevalence of antimeningococcal antibodies in serum (Fig. 2). It was further demonstrated that it was those individuals who *lacked* detectable antibodies to pathogenic strains of meningococci who developed meningococcemia and meningitis upon exposure to meningococci. Individuals with circulating antibodies frequently became carriers of meningococci, but did not develop systemic disease.

Results of these studies also indicated that the development of protective antibodies to *Neisseria meningitidis* occurs as a result of asymptomatic carriage of meningococci in the nasopharynx. Thus, within 2 weeks of acquisition of a strain of meningococci, approximately 90% of normal adults developed high titers of antimeningococcal antibodies. Such antibodies were of the 3 major immunoglobulin classes associated with protection against infectious diseases (IgG, IgM and IgA). In children, where contact with pathogenic strains of meningococci would be expected to result in systemic disease, the carrier state was also found to be important in development of natural immunity. Here, carriage of *avirulent* strains of meningococci seemed to confer cross-reactive immunity to virulent meningococci. It thus appears that natural immunity to

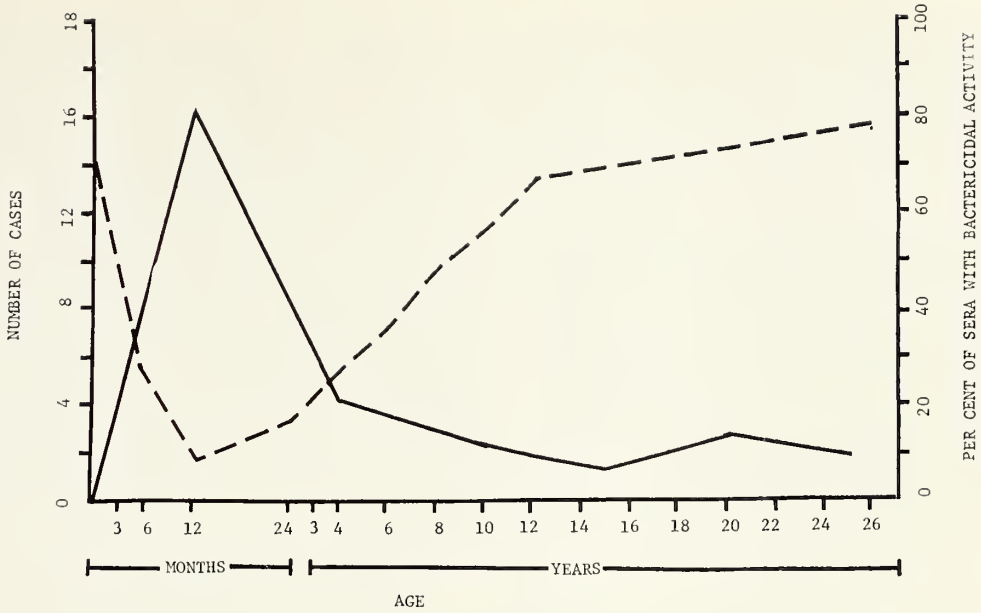

Figure 2

Age-related incidence of meningococcal disease in the United States and prevalence of serum bactericidal antibodies against pathogenic strains of meningococci. ————————, number of cases/100,000 age-specific population, 1966; — — — — — — —, per cent of sera in each age group having detectable bactericidal antibodies against 3 strains of pathogenic meningococci (serogroups A, B and C).

pathogenic strains of meningococci is initiated, reinforced, and broadened by intermittant carriage of different strains of meningococci throughout life.

The antigenic determinants which elicit the immune response to meningococci are diverse. Quantitatively however the more important are the group-specific cell wall polysaccharides and the cross-reactive antigens (probably endotoxin). Antibodies to the group-specific polysaccharides comprise the bulk of immunoglobulins against strains of meningococci that are endemic in a community. For example, antibodies to group C polysaccharide predominate in the United States today, whereas relatively little antibody to group A polysaccharide is present. Protection against group A meningococci introduced into the United States would necessarily derive from cross-reacting antibodies formed against antigens common to meningococci of various serogroups.

The Meningococcal Polysaccharides:

Using a method employing the cationic detergent Cetavlon to precipitate acidic polymers, Gotschlich *et al*[5] were able to obtain highly purified meningococcal group-specific polysaccrarides in large molecular weight form. The polysacchardies are soluble products released into the supernatant by meningococci grown in a chemically defined medium consisting of amino acids, simple sugars and salts.

The group C polysaccharide was found to be an antigenically distinct polymer of sialic (neuraminic) acid—an acetylated arrangement of amino sugars similar to those found in blood group substances and in many glyco-proteins. The group A polysaccharide was identified as an acetylated polymer of mannosamine phosphate, a precursor of sialic acid. The purified polysaccharide preparations contained less than 1% biologically active endotoxin, no protein, and no nucleic acids. They were nontoxic in laboratory animals when administered in large doses. Most importantly, the chemically pure A and C polysaccharides were extremely antigenic in human volunteers and had no significant untoward local or systemic effects.[6]

The stage was thus set for testing the group specific polysaccharides as vaccines against clinical meningococcal disease.[7-9]

Vaccine Field Trials:

To date approximately 20,000 military recruits at 5 army bases in the United States have been immunized with the group C meningococcal polysaccharide and an additional 160 men have received the group A polysaccharide. Results of these field trials are summarized below:

1. *Antibody response.* Intradermal injection of 50μg of group A or C meningococcal polysaccharides resulted in the production within 2 weeks of high titers of bactericidal, hemagglutinating, precipitating, and opsonizing antibodies. The antibodies were of 3 major immunoglobulin classes (IgG, IgM and IgA).

2. *Reactions.* No systemic reactions were observed. Local reactions were minor and varied with the mode of immunization. Intradermal injection of 50μg of either A or C antigen produced a slightly tender zone of erythema 2 to 5 cm in diameter. This appeared at about 8 hours, reached peak intensity by 24 hours, and faded completely by 48 hours. Local reactions to subcutaneous inoculation (needle or air gun) were very mild, consisting of erythema 1.1 ± 0.4 cm mean diameter which faded by 48 hours.

3. *Dose response.* There was a trend of increasing antibody titer with increasing doses of C polysaccharide from 10 to 100μg, although the differences were not satistically significant. However, immunization failures were frequent in the group that received 10μg, whereas all recruits responded in the higher dose ranges.

4. *Route of administration.* Groups of recruits were inoculated by needle with 50μg C polysaccharide via intradermal or subcutaneous routes. A third group was injected subcutaneously with a jet injector apparatus. All responding volunteers developed increased antibody titers within 2 weeks of immunization. There were no statistically significant differences in the titers induced by the various modes of immunization. The air gun was found to be a somewhat less reliable means of immunization when compared to the needle. Depending on the lot of vaccine between 3.5 to 6.5% of recruits failed to show a significant antibody rise in the former groups; whereas less than 3% failed to respond in the latter group.

5. *Effect on meningococcal carrier state.* Intradermal or subcutaneous injection of 50μg group C polysaccharide significantly reduced the carrier rate of group C meningococci. In studies performed among military recruits, 20% of men from several training companies were immunized with the group C antigen. The rate of acquisition of group C organisms among vaccinated individuals was about half that among non-immunized controls. When one considers that the epidemiological pressures to become a carrier of meningococci in military recruit camps are enormous, these results take on added significance. They indicate that systemic immunization with meningococcal polysaccharide results in the development of local (nasopharyngeal) immunity, as well as the production of circulating antibodies. It is possible that immunization of a larger percentage of a population might eliminate the natural reservoir of the meningococcus.

6. *Protection against meningococcal meningitis.* Group C meningococcal polysaccharide was injected subcutaneously (50μg) into each of 13,763 volunteers at 5 army basic training centers. There was an 87% reduction in group C meningitis among the vaccinated individuals (1 case) compared to the attack rate among 54,309 controls (38 proven cases). This result was statistically significant at the 1% level. Since these results were recorded,[8] 10 additional cases of group C meningitis have occurred among controls.

7. *Specificity of response.* Immunization with A polysaccharide produced antibodies only to the A antigen; and C polysaccharide only to the C antigen. Similarly, immunization with the C polysaccharide decreased the carrier rate only of group C meningococci, and protected only against group C meningitis.

8. *Duration of antibody response.* Six of the original volunteers who received both A and C vaccines have been followed for 24 months. Antibody titers (IgG) have remained elevated. This finding is consistent with the experience that human precipitating antibody response elicited by purified polysaccharides is long lasting. Heidelberger reported that detectable antibody to type-specific pneumococcal polsaccharide was frequently present as late as 8 years after immunization.[15]

Comments

Results of the field trials are encouraging. However, it must be stressed that the use of meningococcal polysaccharides as vaccines is still in the developmental stage. While there is no question that the group C polysaccharide would be effective in preventing meningitis in closed populations, it is not known whether immunization would be effective in the civilian population generally. Nor is it known whether purified meningococcal polysaccharides are antigenic in children, who represent the population at greatest risk from systemic disease. Many other questions remain to be answered before these materials can be offered for clinical use.

Several projects designed to provide information of the sort alluded to are planned. These include: 1) Extended use of the group C polysaccharide among military recruits as active prophylaxis against meningococcal meningitis. 2) Large scale field trials of the group A polysaccharide in the "meningitis belt" of Africa under the auspices of the World Health Organization. 3) Limited field studies of group A and C polysaccharides among children in the United States. 4) Preparation of the group B meningococcal polysaccharide in large molecular weight form.

From a more general point of view, and speaking optimistically, should the meningococcal polysaccharides prove effective in the general population they might serve as models for the future development of vaccines against other infectious diseases. The clinical advantages of non-toxic, chemically pure antigens obtained from organisms grown in a non-allergenic medium devoid of complex biological materials are obvious.

Summary

Meningococcal meningitis is a serious disease of childhood, causing significant morbidity and mortality. During periods of mobilization major outbreaks occur among military recruits. At birth, infants are protected by maternally-derived antibodies, but become extremely susceptible to meningococcal infection after the onset of physiological hypogammaglobulinemia. Naturally-acquired immunity appears to result from the asymptomatic carriage of meningococci in the nasopharynx. The bulk of protective antibodies thus formed are directed against the group specific cell wall polysaccharides.

The cell wall polysaccharides of the three major meningococcal serogroups (A, B and C) have been isolated in chemically pure form. All are related to sialic acid, a polymerized amino-sugar. The group A and C polysaccharides have been found to be antigenic in man. Large-scale field trials among military recruits with the group C polysaccharide have been successful in reducing the attack rate of meningitis more than 87 per cent. There were no significant local or systemic side effects. Field studies with the group A polysaccharide and preparation of the group B polysaccharide in antigenic form are contemplated.

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Rubella Vaccine—Some Perspectives

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The history of the development of a live attenuated rubella vaccine represents a triumph for modern day technology since less than seven years has elapsed between the time of the first isolation of rubella virus in an in vitro tissue culture system and licensing of an effective vaccine for general use.

Each of the live virus vaccines which have been developed during the past two decades has had different characteristics and different problems relating to optimal utilization. The demands that are made upon an immunizing agent are stringent and at times, difficult to achieve. There are certain principles that are applicable to all such immunizing agents, however: 1. that they should protect the individual against the disease, 2. that the immunity be as long-lasting as that induced by the natural disease, and 3. freedom from undesirable side effects.

The reasons for prevention and goals in immunization against rubella are different from those associated with poliomyelitis or rubeola. With the latter two disease processes, the rationale is to protect the susceptible individual from a serious or life threatening illness. A second aim is to protect the community (the herd) against the disease by decreasing the reservior of susceptibles.

Rubella is a benign illness with few complications and subclinical natural immunizing infections may be as frequent as clinically recognizable illnesses. If it were not for the known teratogenic properties of this virus, there would be little reason for or interest in the development of a suitable vaccine.

In contrast to rubeola, the acquisition of antibody to rubella during childhood occurs much more gradually and 15-20% of young adult women in the childbearing period may be susceptible. In the U.S. at the present time, there are approximately 200,000 such persons. This is the group that needs the protection now. There is also a decline in natural antibody with time and there is a now a growing body of evidence, such as experimental and clinical data of Horstmann,[1] the clinical data of Brody[2] in isolated population groups and Buescher[3] in recruits which indicate that subclinical pharyngeal reinfection with a booster response in circulating antibody is not infrequent particularly during epidemic periods. During the course of natural infection with Rubella virus, viremia is a constant occurrence. The incidence of viremia during reinfection is not known but probably occurs with lower frequency than during the first infection when large quantities of virus appear in the circulation. Nonetheless, if viremia did occur then a young pregnant woman who becomes subclinically reinfected might still be able to transmit the virus to her fetus. On the other hand, a subclinically reinfected child may shed virus in the throat which in turn could pass to a susceptible mother or teacher who might be pregnant.

How do these unique problems of rubella virus infection relate to the efficacy of rubella vaccine as well as to its distribution?

There are two attenuated rubella vaccines presently licensed for use in the United States, one of which is grown in duck embryo tissue culture and the other in canine kidney cultures. Both are administered parenterally.

All studies have shown seroconversion to occur in over 90% of susceptible subjects following a single dose of vaccine although circulating antibody titers may be lower than those which occur following the natural disease. Persistance of antibody without decrease in titer has been well documented for three years with the expectation that circulating immunity will be long-lasting. Small quantities of virus have been recovered from nasal and pharyngeal secretions of ⅓ to ½ of vaccinees during the first few weeks after immunization. Shedding of vaccine virus is intermittent and transmission to susceptible close contacts has not been found either under institutional conditions or in open population studies. Viremia has been shown to occur in some vaccinated children.[4]

In a controlled investigation in Finland[5] of ten rubella-susceptible women who were vaccinated during the first trimester of pregnancy prior to undergoing theraputic hysterotomy or hysterectomy for sterilization, rubella virus was isolated from placenta of three and from fetal tissue in one in-

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stance. It is not known whether the vaccine is teratogenic; but until further information is available, vaccination is contraindicated in a woman in the childbearing period unless medically acceptable birth control measures are being carried out.

Another problem to be considered is the effectiveness of vaccine virus in preventing infection with natural virus. Wilkins and co-workers[4] challenged vaccinees in an institution with natural rubella virus and found that almost half of such subjects did indeed acquire asymptomatic pharyngeal reinfection with virus shedding and rise in antibody titers. This may be due to the fact that parenterally-administered vaccines may not induce local gamma A antibody which probably plays a large role in local immunity in the respiratory tract. Consequently virus multiplication may occur al-through there will be no symptoms of the disease. Whether such a vaccinated and reinfected individual would undergo viremia is not known; but because circulating neutralizing antibody is present, the risks again should be less than that which occurs with natural rubella infection. However, they did shed virus in the throat which could pass to susceptibles.

With the present limited supply of the vaccine and the prospects of an epidemic within the next two years, recommendations of the Unittd States Public Health Service Advisory Committee on Immunization Practices[6] are for administration of vaccine to children from one year to puberty, emphasizing kindergarten and primary grade children, since they are the chief disseminators of the disease during epidemic periods. The goal is to protect the 200,000 women at risk by eliminating the reservoir of susceptible children who would expose them to the virus.

As soon as adequate quantities of vaccine become available, the only practical approach is to carry out such immunizations as rapidly as possible through community programs. Federal funds have been designated to provide vaccine to state health departments which can distribute it to city health departments requesting it. Infants less than one year may still have some persisting maternal immunity and might not respond optimally to the vaccine. Community protection can be maintained by inclusion of rubella vaccine into well child immunization programs. Buynak and co-workers[7] have developed a single-dose preparation consisting of a mixture of attenuated rubeola, mumps, and rubella vaccines. It is free of side effects and is as effective in inducing seroconversion to all three types of virus as each vaccine individually. Such a preparation could be administered once to children at age of one year and protect them against all three diseases.

It is possible that other types of vaccine such as the intranasal preparation developed by Plotkin[8] will supercede the parenteral vaccines now available. Theoretically, such a vaccine could eliminate the problem of nasopharyngeal reinfection by inducing local antibody formation.

At present in order to assure protection to young women in the childbearing period, it would be desirable for a physician to first submit a serum sample to a reliable laboratory to be examined for presence of rubella antihemagglutinating (HAI) antibody and then offer vaccine to those who are susceptible if pregnancy prevention is assured for two months following immunization. The woman should understand that she might still become infected with rubella virus during an epidemic period but the likelihood of transmission of such virus to an unborn fetus would be much less. It should be remembered that transient arthritis has been reported to occur following administration of attenuated vaccine.[9]

There is a high risk group of women who should be reached now. These include physicians, nurses and paramedical personnel who care for newborn infants. If susceptible, they may acquire rubella from infants with congenital rubella syndrome who frequently shed large quantities of virus for many days or weeks after birth in throat, feces, urine, tears. It would seem appropriate for hospitals to offer screening for susceptibility and vaccination if indicated to all such women employees. Other women who may be vulnerable include school teachers, nurses and medical personnel and many who care for sick children in offices, clinics, and emergency rooms.

Equally important is a surveillance program emphasizing improved diagnosis and reporting of rubella and congenital rubella syndrome. Patterns of vaccine use should be monitored. Physicians should insist upon laboratory invesitgations on all infants with birth defects suspected of being due to rubella so that the incidence prevalance can be determined, and likewise effectiveness of vaccination can be assessed. Rubella and congenital rubella syndrome are reportable to local health officers.

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Responsibility Of Team Physicians

The following statement, drafted by the Committee on Accident Prevention and approved by the Council, has been accepted by the Football Committee of the Connecticut Interscholastic Athletic Conference:

"It shall be the responsibility of the physician in attendance at all CIAC athletic contests to decide whether a player is or is not physically fit to participate in the game. The decision of the physician in attendance shall supersede that of any official, coach or other school personnel."

Infection of the Urinary Tract

George W. Lewis, M.D.

Four entities attributible to infection of the urinary tract are quite common in human females. These are: (1) acute cystitis, which is an acute infection of the urinary bladder which will run its course even without antimicrobial therapy; (2) acute pyelonephritis which may be found at any age, but which is certainly more common in women of the child bearing age, and especially in pregnant women; (3) asymptomatic bacteriuria in either pregnant or non-pregnant women; and (4) chronic pyelonephritis which may be appreciated clinically, but is largely an autopsy diagnosis. The latter is not uncommonly seen in women who have no history of acute cystitis or of pyelonephritis, and who may have normal urine cultures even shortly before their demise. It is not possible at this juncture to trace the natural history of urinary tract infections in women from symptomatic or asymptomatic infections to end stage chronic pyelonephritis. There are indications, however, that bacteriuria is associated with a high incidence of abnormalities of kidney function in women.[1, 2] This, along with the recent demonstration of bacterial antigen in a high percentage of people with a pathological diagnosis of chronic pyelonephritis,[3] is certainly strong presumptive evidence that a rigorous approach to symptomatic and asymptomatic infections of the female urinary tract may prevent long term damage from chronic pyelonephritis.

Infections of the male urinary tract are even more difficult to evaluate in terms of their long term significance. In the first place, symptomatic infections of the male urinary tract do not occur frequently. With the exception of the various types of urethritis, infection of the male urinary tract does not occur with any frequency until relatively late in life when prostatism and diabetes mellitus are much more common. In fact, it is quite uncommon to see acute, symptomatic cystitis or pyelonephritis in the male in the absence of anatomic abnormalities which contribute to the obstruction of the normal flow of urine. There is also a paucity of information about the incidence of asymptomatic bacteriuria in the male.[4]

There are, then, several distinct entities which involve infection of the urinary tract. At the moment it is not possible to establish the connection between thest various entities with any degree of certainty. These can be divided as follows: (1) Cystitis and/or acute pyelonephritis in the female, (2) asymptomatic bacteriuria in the pregnant female, (3) asymptomatic bacteriuria in the non-pregnant female, (4) urinary tract infection associated with obstruction of urine flow in males and females of all ages, (5) chronic bacteriuric pyelonephritis in the female, and (6) chronic, non-bacteriuric pyelonephritis which is usually an autopsy or biopsy diagnosis. It is important to recognize the difference in these types of infection of the male and female urinary tract because the approach to therapy is different in each. The pathogenesis of the various types of urinary tract infection may also be different, but an understanding of the known facts in the pathogenesis of urinary tract infection is important in understanding the course of infections of the urinary tract and in establishing a rationale for therapy. I will, therefore, present a very brief discussion of the experimental and clinical data which contribute to our understanding of the pathogenesis and therapy of the various types of urinary tract infection.

Infection of the urinary tract in animals can be produced experimentally by two different routes. The first is the hematogenous route. If the proper level of bacteremia is achieved, bacteria can regularly be recovered from the kidneys of animals for varying times after the initiation of bacteremia. As a corollary in the human, bacteriuria is frequently seen during the course of bacteremia. In most experimental animals, this type of kidney infection does not usually result in bacteriuria and is usually terminated within one to two days by mechanisms which are not at all well understood, and no microscopic lesions are produced in the kidneys.[5] If the infection is produced by the proper bacteria, however, microscopic evidence of infection as well as bacteriuria may occur.[6,-7] Evidence of progressive, though self limited, infection in the kidney may be produced by most bacteria if any of several mechanisms are used to alter the normal function of the kidney.[8, 9] How these mechanical alterations affect the fate of bacteria in the kidney is not understood.

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Several facts are, however, apparent from these clinical and experimental studies: (1) bacteria in the blood are regularly filtered into the kidney, (2) in the normal kidney most bacteria do not cause structural damage or progressive infection, (3) certain bacteria will produce structural damage and infection even in normal kidneys, and (4) alterations in kidney dynamics, and particularly obstruction to urine flow (either intra- or extrarenal) will render a kidney susceptible to infection by bacteria which might otherwise cause only transient infection.

The second method of producing experimental infection of the urinary tract in animals involves inoculation of bacteria into the urinary bladder. As one might expect, this usually results in a transient bacteriuria. Persistent urinary tract infection with histologic changes can be produced by such mechanical means as placing glass beads in the bladder or producing partial obstruction of a ureter. A major implication of these experimental studies is that the whole system is remarkably resistant to infection. Urine itself has been shown to have some bactericidal capacities; the bladder is felt to inhibit bacterial growth, and the unobstructed flow of urine is felt to prevent the accumulation of large numbers of bacteria. These studies help a great deal in understanding the pathogenesis of urinary tract infection where the flow is obstructed, either in the kidney, in the bladder, or in the urethra. They contribute little, however, to our understanding of why normal females may suddenly have an attack of cystitis or pyelonephritis; and they certainly don't contribute at all to our understanding of the phenomenon of non-bacteriuric pyelonephritis.

The brief discussion of the pathogenesis of infection of the urinary tract presented above will serve as an introduction to the rationale for the treatment of such infections. In this discussion the selection of antibiotics will not be dwelt upon, but will be mentioned . A special attempt will be made to relate the therapy to the pathogenesis of the particular type of infection.

As has been mentioned above, both acute cystitits and pyelonephritis are self-limited diseases the pathogenesis of which is very poorly understood. Persons suffering from these afflictions will almost always improve whether therapy is given or not. The acute nature of the affliction with the severe discomfort of cystitis and the pain, fever, vomiting, and systemic manifestations of pyelonephritis do, however, make antibiotic therapy almost mandatory. These infections are usually the result of *Escherichia coli* which are sensitive to most antimicrobials. Those most widely used are sulfisoxizole, the tetracyclines, ampicillin, nitrofurantoins. There is no evidence that any one of these is superior to the other. The effects of tetracycline on bone growth, tooth formation, and possibly on hepatic function in pregnant women make one of the other agents more advisable in pregnancy. Usual doses of these agents are quite effective. Acute pyelonephritis is often accompanied by severe systemic manifestations such as fever, pain, nausea, and vomiting. The latter two, especially, may warrant a brief hospitalization for hydration and parenteral administration of antibiotics until the acute symptoms have subsided. The duration of therapy need not be long. Seven to ten days will usually suffice.[10] Urine cultures should be obtained prior to the institution of antimicrobial therapy, and the agent adjusted, if necessary, when the sensitivity of the offending organism is known.

Perhaps the most important aspect of the treatment of acute cystitis or pyelonephritis is the follow-up which the patient receives. We certainly do not have sufficient understanding of the natural history of an episode of acute urinary tract infection to warrant dogmatic statements; but the best available evidence today would indicate that the discovery of persistent or recurrent bacteriuria is worth the effort and expense involved. In fact, as non-cultural methods for the detection of bacteriuria become perfected, the expense will probably be drastically reduced.[11, 12] At the moment I would recommend a repeat culture within the first two weeks of the cessation of antibiotic therpy, and subsequent cultures at less frequent intervals for one or two years after the acute episode. One should always remember that chronic bacteriuria may not be a constant phenomenon, and should not be lulled into a false sense of security by a single negative culture.

Recurrance of bacteriuria, as evidenced by two or more cultures showing significant numbers of bacteria indicates a different approach. If the organism is different from the pathogen originally isolated during the acute attack, then a reinfection is assumed and another ten to fourteen day course of therapy with an antibiotic selected on the basis of sensitivity tests should be given. If, on the other hand, the same organism is isolated from the follow-up specimen a persistent infection is indicated, and therapy should be given for a much longer period of time. The actual duration of therapy is not known, but should be not less than six to eight weeks, and possibly longer.[13] The rationale behind the recommendation of this long course of therapy is that persistent infection usually implies some degree of scarring of the kidney, and, as we have seen, this predisposes to infection and contributes to the difficulty of eradicating bacteria from the kidney. Recurrance of or persistance of bacteriuria after the treatment of an acute infection should always indicate a search for structural defects which might be responsible for the infection. This should at the barest minimum consist of an IVP, and should ideally involve a complete urologic evaluation.

There is a significant problem involved in the above approach. There are many serologic types of *E. coli,* the most common etiologic agent in acute cystitis and pyelonephritis. Most clinical laboratories are not equipped to perform serologic identifications of E. coli and may not, therefore, be capable of telling the clinician whether or not the newly isolated organism is actually the same as the original isolate. Antibiotic sensitivity patterns should be used with caution for this purpose since gran negative bacilli can easily become resistant to most antibiotics. Under these circumstances the clinician may wish to modify the recommended approach and wait for even a third recurrance with the same organism before initiating a long term course of therapy. This should not, however, modify his resolve regarding diligent long term follow-up of an acute, and especialy of a recurrent episode of cystitis or pyelonephritis.

The adverse effects of symptomatic bacteriuria in pregnancy have been stressed many times over. The facts are that the incidence of many complications of pregnancy for both mother and fetus are increased in the presence of bacteriuria.[14] Treatment of this condition is certainly warranted when it is found. The choice of the antibiotic in this instance should be dictated by the sensitivity patterns of the organism isolated and the safety of the agents for both mother and fetus.

There is not at present any agreement as to the value of routine cultures of the urine in women or men. As mentioned above, the perfection of non-cultural methods for the detection of bacteriuria should make this evaluation a part of every routine urinalysis. When this is possible, information should be forthcoming regarding the real incidence of bacteriuria in the population and the natural history of this condition. There is, however, evidence that bacteriuria does produce defects in concentrating ability of the kidney and that elimination of bacteriuria does result in a restoration of normal function. Since reversible functional defects do accompany asymptomatic bacteriuria treatment is certainly warranted when the condition is discovered. The choice of the antibiotic will, once again depend on the sensitivity pattern of the organism isolated.

As in the case of acute urinary tract infections, follow-up for treatment of asymptomatic bacteriuria may well be the most important aspect of the therapy. If the infection cannot be eradicated easily, or if infection recurs long-term therapy should be initiated, and a diligent search made for correctible structural abnormalities which might prevent recurrance. This latter is especially important. We may not know the natural history of asymptomatic infection in the absence of obstruction, but it is axiomatic that infection plus obstruction will result in destruction of renal tissue.

The above axiom is especialy applicable when one considers urinary tract infection in either the male or female which is secondary to obstruction. Obstruction at any point in the urinary tract renders the proximal tract particularly susceptible to infection. Once it occurs, infection in the obstructed urinary tract is extremely difficult to eradicate. Relief of the obstruction is the aim of any initial therapy. This will usually require surgical correction of the defect. Antimicrobial therapy should be approached with caution until the obstruction can be relieved. The clinician should realize that eradication of infection is dependent on relief of obstruction and should aim, rather at descreasing the numbers of bacteria in the urine. For this purpose long term administration of nitrofurantoins or mandelamine may suffice for susceptible organisms. More potent antimicrobials should be reserved for crisis situations or for therapy when the obstruction is relieved. The clinican should also remain acutely aware that the patient with urinary tract obstruction is an excellent candidate for gram negative bacteremia or sepsis. He should remain familiar with the organisms in the patient's urine, and, especially following instrumentation of the urinary tract, should be prepared to initiate appropriate therapy when the clinical course indicates that an acute infection is present. A detailed discussion of the therapy of gram negative bacteremia is beyond the scope of this paper, but careful attention to the patient with known obstruction of the urinary tract should prevent the more serious aspects of this problem. When thinking of antibiotics in this situation one should rely on parenteral administration and should consider more potent agents such as cephalothin, kanamycin, colistin, gentamicin, and chloramphenicol. A prior knowledge of the sensitivities of the organisms present in the patient's urine can serve as an excellent guide to therapy in a crisis situation.

When infection of the urinary tract accompanies systemic conditions such as diabetes mellitus and lupus erythematosis the physician must exercise his judgment. When infections are first discovered, they should be treated diligently as outlined above. One must often face the realization in these patients as well as in some with chronic pyelonephritis without demonstrable cause, that he will not be able to eradicate the infection. At this point continued administration of increasingly toxic antibiotics on the basis of the sensitivity of the most recent isolate is folly, the end result of which will be infection with an organism resistant to all but the most toxic agents. Quite possibly renal damage from some of the agents used will precipiate renal failure. As in the case of a patient with obstruction which can't be relieved the physician must learn to live with an infected urine and must set his goals at a level of reducing the level of bacteriuria and of preventing or treating bacteremia.

Too much has already been written about the urinary catheter and infection to leave much doubt in one's mind that such devices result in such a complication. Even using the best technique and equipment, infection of the urine cannot be delayed much more than two to three weeks when an indwelling catheter is in place. Infection of the urine may not, however, be the greatest problem which a patient may face, and a decision to use an indwelling catheter may have to be made. In medicine we are not infrequently faced with a choice between less than ideal situations and must learn to live with our imperfection. If, in fact, long term drainage of the urinary bladder is anticipated, a cystotomy or leal loop procedure may be superior to a permanent indwelling catheter. When infection occurs in such situations, however, the treatment of choice is to maintain as free as possible a flow of urine in relatively large volume. Antibiotics will again be useless except for treatment of acute episodes of pyelonephritis or bacteremia.

In summary, acute cystitis or pyelonephritis can usually be treated adequately with oral antibiotics. Symptomatic improvement is to be expected, and follow-up is crucial. Attempts should be made to eradicate asymptomatic bacteriuria whenever it is identified with therapy similar to that for acute infections. And finaly, when one is faced with any of a number of situations in which elimination of bacteria from the urine is not possible one should learn to accept the presence of bacteriuria and to try to reduce the incidence of complications.

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Usefulness of Gram Stain and Routine and Quantitative Culture of Sputum in Patients With and Without Acute Respiratory Infection

Raymond C. Bartlett, M.D. and Avrohm Melnick

The interpretation of cultures of sputum in diagnostic microbiology laboratories is made difficult by the numerous species of mixed flora and potential pathogens that are observed. There is always concern that mixed bacterial flora may obscure the presence of important potential pathogens. The term "mixed flora" has been applied to the alpha hemolytic streptococci, Neisseria species, Corynebacterium species other than C. diphtheriae, and Staphylococcus epidermidis. Various gram negative bacteria are frequently found in sputum specimens and usually represent colonization without infection. However, these organisms may cause acute pulmonary infection and must be reported. Klebsiella pneumoniae should be distinquished from other coliform bacteria because they are associated with a higher incidence of infection in the respiratory tract. In addition to the criteria required for such differentiation, the varying antimicrobial susceptibility patterns require susceptibility testing. Examination of a gram stain of the sputum specimen frequently provides an initial impression of the presence of potentially pathogenic organisms which may be related to respiratory infection and is considered by most to be a useful preliminary guide to the bacteria that may be recovered on culture. A technique that would eliminate non pathogenic or colonizing bacteria and focus attention on identification and susceptibility testing of clinically important potential pathogens would make much more efficient use of diagnostic bacteriologic services.

Homogenisation and quantitative culture of sputum specimens has been suggested as a method of accomplishing this.[1-3] Reports of this technique have shown that organisms associated with infection will be present in larger numbers than those representing colonization or mixed non pathogenic flora. With or without washing of sputum, it has been reported that bacteria associated with secretion in the oropharynx would be diluted out by the procedure. Louria[3] concluded that the quantitative method had limited application and could produce misleading results in chronic pulmonary disease and be significantly influenced by relatively high counts of bacteria present in the oropharynx.

The proper collection and transmission of specimens and the prompt inoculation of purulent appearing portions on appropriate bacteriologic media are essential to conventional bacteriologic analysis of sputum. Practical limitations dictate that delay frequently occurs, that specimens are frequently highly contaminated with oropharyngial material and that careful sampling of the most significant portion of the specimen is not always accomplished. Washing of sputum specimens or rinsing of the mouth may help reduce contamination from bacteria in the oropharynx. Dixon and Miller[1] compared homogenization and quantitative culture of sputum with the results obtained following routine culture of washed sputum specimens. They concluded that the approach greatly simplified the routine analysis of such specimens since mixed flora was greatly reduced and that either pure cultures of single pathogens were observed or no-growth occurred. These authors undertook no correlation with clinical evidence of respiratory infection in their study.

An investigation was established in this laboratory to compare the results of examination of gram stains, routine methods of sputum culture, and homogenization and quantitative culture of sputum specimens. We wished to determine:

1. Does homogenization and quantitative culture of sputum detect more pathogens than the rou-

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tine method in patients with acute respiratory infection?

2. Does the quantitative method decrease the number of bacteria representing mixed non pathogenic flora and potential pathogens in patients without evidence of acute respiratory infection?
3. How well does the gram stain correlate with culture results?
4. How well does the presence of potential pathogens observed in the gram stain correlate with the presence or absence of symptoms and signs of acute respiratory infection?

Materials and Methods

Dithiothreitol,[4] N-acetyl-L-cysteine, and pancreatin were compared as possible agents for liquifaction of sputum. Dithiothreitol marketed as sputolysin© appeared stable and produced rapid liquifaction and homogenization. Previous difficulty in this laboratory with instability of N-acetyl-L-cystine lead to disfavor as an alternative reagent. Pancreatin requires a longer digestion period and was rejected for this reason.

One hundred and ninety two consecutive specimens were evaluated. Cultures of these specimens were ordered by physicians in the course of evaluation of respiratory infection in hospital patients. The procedure consisted of preparation of a gram stain and inoculation of a selected purulent appearing portion of the specimen using a wire loop onto a blood agar plate consisting of trypticase© soy agar* containing 5% defibrinated sheep blood and MacConkey medium. The blood agar plate was routinely streaked with Staphylococcus aureus to provide a source of NAD for satilitic growth of Hemophilus influenzae. This procedure was performed within two hours of collection of specimens. Specimens were refrigerated and subsequently analysed by the quantitative method after a period of no more than six hours storage at 4-8°C. This involved transfer of the specimen to a calibrated glass centrifuge tube to which was added an equal volume of a solution of dithiothreitol prepared by adding 10 ml. of the material supplied by the manufacturer to 100 ml. of isotonic saline.** This was treated on a vortex mixer for several minutes during which time liquifaction occurred. It was centrifuged and the supernatant was discarded. The resulting pellet was resuspended in sterile physiological saline solution.** This suspension was diluted to 10^{-4}, 10^{-5} and 10^{-6} with the same sterile diluent. 0.1 ml. amounts of each dilution was deposited on a chocolate agar plate (tripticase© soy agar containing 5% chocolatized horse blood and 1 ml. of enrichment)*** and a blood agar plate (tripticase soy agar with 5% defibrinated horse blood) and a MacConkey agar plate. The inoculum was spread over the surface of each plate using a bent solid glass rod spreader.

Both sets of plates were incubated in a capneic incubator at 35-36°C in an atmosphere of 5-10% CO_2 at 70% humidity. Plates from each procedure were evaluated by separate personnel neither of whom had knowledge of the results of examination by the other. Isolates were identified by colonial appearance, gram stain morphology, and standard biochemical tests.

Clinical data was collected on each patient at the time the specimen was submitted. This included the primary diagnosis, radiologic observations, production of sputum, and nature of such secretions as well as ascultatory evidence of pneumonitis, evidence of fever, and leukocytosis.

Neisseria species, Corynebacterium species excluding C. diphtheriae, Streptococci other than Streptococcus pyogenes, and micrococci excluding Staphylococcus aureus were collectively reported as mixed flora in both procedures. Since all specimens were collected from adult patients, the clinical significance of isolation of Hemophilus influenzae was considered questionable. In the routine procedure, evidence of satilitic growth on blood agar plates streaked with Staphylococcus aureus yielded a report of Hemophilus influenzae. Hemophilus species isolated by the quantitative method were grouped with the mixed flora.

Specimens were placed in three categories based on the clinical status of the patients. Group 1 consisted of patients with definite evidence of respiratory infection. Most had X-ray evidence of pulmonary infiltration, several positive auscultatory signs, fever and produced moderate amounts of purulent sputum. Group 2 contained those patients showing some evidence of infection. Group 3 contained those patients with no evidence of acute respiratory infection. Although this third group of patients had produced sputum which was submitted for culture, clinical problems usually represented asthma or chronic bronchitis with no evidence of an acute respiratory infection.

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* BBL, division of BioQuest

** McGaws Physiological Saline

*** Isovitalex©, BBL division of Bioquest

Group	Characteristics	Number of Specimens
1.	Acute respiratory infection	69
2.	Possible acute respiratory infection	68
3.	No acute respiratory infection	55
	Total	192

In a comparison of the observations made on sputa from these clinical groups it seemd desirable to eliminate Group 2 since it was doubtful that the presence or absence of infection in these patients could be established confidently. Cultures were defined as positive when one or more potential pathogens were isolated. This included Diplococcus (Streptococcus) pneumoniae, Staphylococcus aureus, Streptococcus pyogenes, Klebsiella pneumoniae, Enterobacter species, Escerichia coli, Proteus species, Pseudomonas aeruginosa, and miscellaneous gram negative bacteria. Negative cultures were defined as those showing no bacterial growth or mixed flora.

Results

Tables 1 and 2 demonstrate a larger number of positive cultures by both methods in the infected group of patients. In patients without infection, a somewhat larger number of negative cultures was obtained by both methods. No significant difference was observed in the numbers of positive and negative cultures obtained by the routine versus the quantitative technique in either group of patients. In both groups of patients it may be seen that a progressive decrease in the number of pathogens which were isolated occurred in the presence of mixed flora as progressive dilution was performed. A corresponding increase in negative specimens is seen for both patient groups with increased dilution. Table 3 demonstrates a smaller number of pathogens isolated by the routine method alone as compared to the quantitative method alone in both patient groups, but the difference is not statistically significant.*

TABLE 1

Potential Pathogens	*Routine Culture*	*Quantitative Culture* 10^{-4}	10^{-5}	10^{-6}
Detected				
Without mixed flora	14	15	16	16
With mixed flora	37	36	30	14
Mixed flora alone	18	18	22	28
No growth	0	0	1	11
Total Positive Specimens	51	51	46	30
Total Negative Specimens	18	18	23	39

Incidence of positive and negative cultures from specimens received from patients with evidence of pulmonary infection. Comparison of results of routine method and three dilutions using homgenization and quantitative culture shows no statistically significant difference in the number of positive and negative cultures.

TABLE 2

Potential Pathogens	*Routine Culture*	*Quantitative Culture* 10^{-4}	10^{-5}	10^{-6}
Detected				
Without mixed flora	11	13	13	11
With mixed flora	23	18	16	6
Mixed flora alone	20	22	20	24
No growth	1	2	5	13
Total Positive Specimens	34	31	29	17
Total Negative Specimens	21	24	25	37

Comparison of results of routine and quantitative culture of sputum specimens from patients without evidence of pulmonary infection reveals no significant difference in the number of positive and negative cultures by either method.

TABLE 3

	Method of Culture		
Patient Group	*Routine Only*	*Quant. Only*	*Both Methods*
Infection (69)	34	40	38
No Infection (55)	19	22	27
Total (124)	66	88	89

Distribution of 243 potential pathogens which were detected in 124 specimens demonstrates no statistically significant increase in the number found by the quantitative method over those found by the routine method in patients with evidence of infection or in patients without evidence of infection.

There was no evidence that any particular potential pathogen was isolated more frequently by either method. In table 4, the incidence of isolation

TABLE 4

Pathogens	*Infection*	*No Infection*	*Total*
D. pneumoniae	22	24	54
(Hemophilus sp.	*24*	*9*	49)
Klebsiella	*20*	*9*	40
Strep. pyogenes	13	9	34
E. coli	*17*	*6*	28
Pseudomonas	12	5	20
Enterobacter sp.	8	3	15
Staph. aureus	4	4	14
Proteus	7	6	14

Distribution of individual pathogens isolated by both routine and quantitative methods in patients with and without evidence of pulmonary infection. Underscored values are statistically significant at the .90 probability level (Chi square >2.71) but not at the .95 probability level (Chi square >3.84).

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* Chi square <3.84

of potential pathogens from both groups of patients is shown. Diplococcus pneumoniae was the most frequently isolated potential pathogen, but it was found with equal frequency in both groups of patients. Statistically significant increases occurred in the numbers of Hemophilus species, Klebsiella pneumoniae, and E. coli isolated from the infected group of patients.

Table 5 summarizes the results of examination of gram stains compared to cultures. D. pneumoniae was suspected in the gram stain in 53 specimens. In 37 of them, this agent was subsequently cultured. In 13 instances, D. pneumoniae was cultured from specimens in which gram stains failed to suggest their presence. In table 6 it may be seen that the probability of culturing D. pneumoniae from specimens in which gram stains suggested their presence was no different among patients with definite evidence of respiratory infection and those without evidence of infection. The incidence of identification in gram stains or isolation in culturt of D. pneumoniae was not significantly different in either group of patients.

TABLE 5

Agent	*Suspected on Gram stain alone*	*Isolated by Culture† only*	*Suspected on Gram strain and isolated by culture†*
D. pneumoniae	29	13	24
Staph. aureus	71	2	7
Gram neg. rods	60	18	52
Hemophilus sp.	33	3	8

Comparison of results of inspection of gram stains with results of culture in all specimens.

†Routine or Quantitative

TABLE 6

	Gram Neg. Rods		*D. pneumoniae*	
	Infected	*Not Infected*	*Infected*	*Not Infected*
Gram stain pos.	44(86%)	29(100%)	21(75%)	14(70%)
Culture* pos.	32(63%)	15(50%)	20(70%)	11(55%)
Culture* pos/ gram stain neg.	7(14%)	0(0%)	7(25%)	6(30%)
Gram stain pos/ culture* neg.	19(37%)	14(50%)	8(29%)	8(40%)
Gram stain and culture* pos.	25(49%)	15(50%)	13(46%)	6(30%)
Total	51	29	28	20

Comparison of gram stain results with cultures in patients with and without evidence of acute respiratory infection.

*Quantitative or Routine Culture

Micrococci consistent with Staphylococci were frequently seen in gram stains, but Staphylococcus aureus was rarely isolated.

Gram negative rods of the type suggesting Pseudomonas or Enterobacteriaceae were seen in gram stains from sputum of patients in both groups (table 6). In nearly half the instances cultures failed to isolate such agents from these specimens. It is of interest that positive cultures did not occur when the gram stain failed to demonstrate gram negative rods in the uninfected group of patients. Cultures were usually negative when gram stains were negative in the non infected group.

Comments

No increase in the number of positive cultures or in the number of pathogens detected was observed with tht use of the quantitative method in the examination of specimens from patients with probable pulmonary infection as compared to patients without evidence of acute infection. Furthermore, there was no reduction in the isolation of mixed flora in specimens from either group by the quantitative technique. As in the report of Dixon and Miller, there was an increase in the number of specimens showing no growth in both the infected and non-infected group, but this would appear to be the result of dilution. A simultaneous reduction in the number of potential pathogens detected from specimens from infected patients occurred when dilutions up to 10^{-6} were used in order to obtain a significant increase in cultures showing no growth. It is not surprising that almost twice the number of potential pathogens were isolated from patients with clinical signs of acute respiratory infection than from patients without such symptoms.

It is interesting that D. pneumoniae was isolated as frequently from patients with evidence of infection as from patients without evidence of infection. Significant differences could be attached to the difference in the frequency of isolation of Hemophilus species, Klebsiella pneumoniae, and E. coli from patients with and without evidence of acute respiratory infection.

It is apparent that gram stains of sputum reveal D. pneumoniae as frequently in both infected and non infected groups of patients and provide no clue to the likelihood of subsequent isolation of this agent. Gram negative rods are commonly seen in gram stains of sputa from both groups of patients, but cultures were found positive in about half of these and bore no relation to evidence of acute infection. Cultures were usually negative when gram negative rods were absent in gram stains.

Conclusion

The isolation of potential pathogens from sputum specimens results in the expenditure of extensive bacteriological effort in speciation and susceptibility testing which may not be clinically relevant. Gram stains, homogenization, and quantitative cultures of sputum specimens were studied to determine whether either procedure in comparison with the routine method of culture would assist in excluding mixed non pathogenic flora and insignificant numbers of potential pathogens from unnecessary bacteriologic evaluation. Homogenization and quantitative culture failed to reduce the frequency of mixed non pathogenic flora in specimens and failed to reduce the frequency of isolation of potential pathogens from patients without evidence of acute pulmonary infection or increase their incidence when there was evidence of such disease. Homogenization and quantitative culture should be used in selected situations where specimens can be carefuly collected and serially examined and does not constitute a useful replacement for routine methods of culture of sputum specimens. The investigation demonstrated that gram stain did not correlate with culture results or evidence of acute infection with regard to D. pneumoniae. Absence of gram negative rods in gram stains was associated with negative cultures.

The authors wish to acknowledge the assistance provided in this study by Mr. George Carrington, Microbiologist; and Mrs. Virginia Wickersham, R.N., Nurse Epidemiologist.)

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Announcement

National X-Ray Exposure Study

The Public Health Service will conduct a national study to obtain information on population exposure to diagnostic and therapeutic X-radiation. It will begin on April 13th and will be made jointly by the Bureau of Radiological Health and the National Center for Health Statistics. The study was planned with the advice of a group of radiologists and physicists representing the American College of Radiology.

The 1970 study will use the same collection and analysis methods employed in the 1964 survey so that results of the investigations will be directly comparable. This will afford the opportunity to evaluate the effectiveness of programs to improve X-ray practice and reduce unnecessary exposure. The 1970 study also will aid in establishing guidelines for future programs.

MORRIS A. GRANOFF, M.D.
President

Born, Newark, New Jersey, March 20, 1914

Married—Dorothy E. Rosenstock

Children—Susan Margaret, Hollis Barbara, Phyllis Emily, Andrea Ilene

Education—
    Public Schools of New York City
    Townsend Harris Hall High School 1928
    College of the City of New York 1928-31
    University of Oklahoma 1932-1933 (AB 1933)
    School of Medicine, Division of Biological Sciences
        University of Chicago 1933-37 (M.D. 1937)
    Dept. of Public Health, Yale Medical School 1950-52 (MPH 1952)

Hospital Training—
    Nathan Littauer Hospital, Gloversville, New York 7/1/37-6/30/38
    Willard Parker Hospital, New York, N.Y. October-December 1938
    Harlem Hospital, New York, N.Y. January 1939-December 1940

Private Practice—(General Medicine)
    New Haven, Connecticut, January 1941-1944 and 1946-present

Military Service (Captain, A.U.S.), 1944-1946

Associate in Medicine, Yale-New Haven Hospital

Physician, Bureau of Communicable and Venereal Diseases,
    New Haven Dept. of Health, 1943-44, 1946-53 (Acting Director 1951-52)

Member, New Haven Board of Health Commissioners, 1955-60

Medical Director, (part-time) A. C. Gilbert Co., 1953-66

Medical Director, (part-time) Conn. Hard Rubber Co., 1956-Present

Delegate, New Haven County Medical Association, 1959-1967

Associate Councilor, New Haven County Medical Association, 1967-69

President Elect, Connecticut State Medical Society, 1969-70

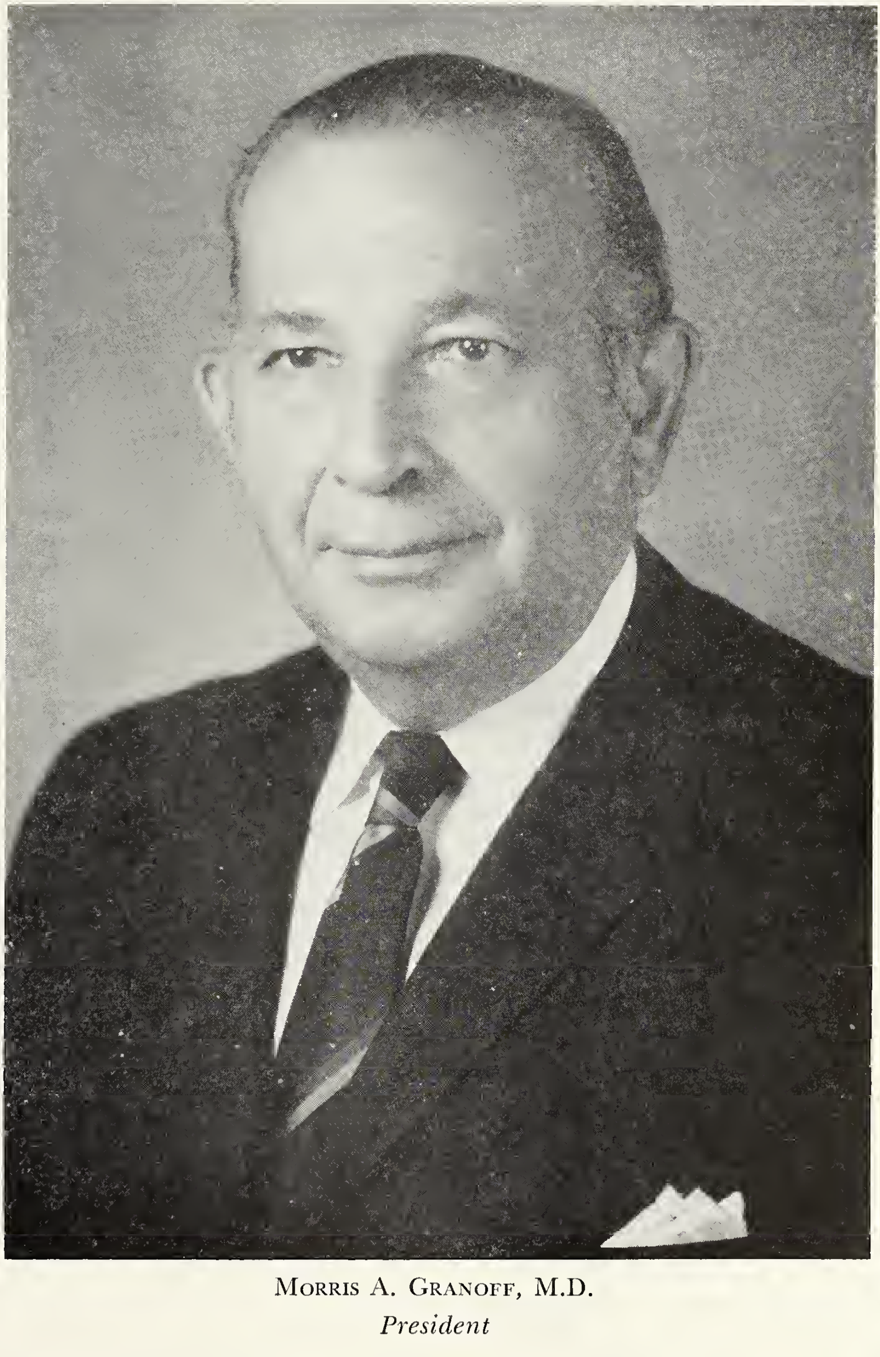
President Elect, President, Conn. Industrial Medical Association, 1964-66

Delegate to Industrial Medical Association, 1965-68

Vice President, New Haven Medical Association, 1969

President, New Haven Medical Association, 1970

Member—
    American Medical Association
    Connecticut State Medical Society
    New Haven County Medical Association
    New Haven Medical Association
    American Public Health Association
    Royal Society of Health
    Connecticut Industrial Medical Association
    Industrial Medical Association
    American Geriatrics Society (Fellow)



Morris A. Granoff, M.D.
President

THE PRESIDENT'S PAGE

As your newly-installed President I want to express my thanks for the honor which has been bestowed upon me and for the opportunity to serve the membership of the Society. This is your organization and it is only as strong as you make it and as effective as you want it to be. Its effectiveness is directly proportional to the participation of the membership in the affairs of the Society and the degree to which the membership is informed. The Society has many committees, both "standing" and "ad hoc"; some are elected and others are appointed. There is much untapped talent among our members which could be used to great advantage by these committees. The question has been how to find it. Several years ago I suggested that a questionnaire be sent to the members soliciting volunteers for these assignments. This was in the form of a tear-out page in *Connecticut Medicine*. The response was gratifying and I hope it will be done each fall before the Committee on Preliminary Study of Nominations meets to draw up the slate for the coming year, which will include the nominees for all Standing Committees.

Keeping the membership informed of the activities of the Society and the problems facing the profession locally, statewide, and nationally is most difficult. At the national level, the *JAMA* and the *American Medical News* do a good job of providing information to the AMA members. In Connecticut, the Society publishes a monthly scientific Journal, *Connecticut Medicine*, a bi-monthly newspaper, *Connecticut M.D.*, and recently started to publish a bi-monthly newsletter, *CSMS Newsletter*, between issues of *Connecticut M.D.* At the County level, both Fairfield and Hartford Counties operate active programs to keep their memberships informed. New Haven County is embarking on a Public Relations program which will attempt to provide better communication between the Association and its members and with the general public. In spite of all these efforts, all too many members are not as well informed as they should be.

The House of Delegates, at its semi-annual session in December, 1969, created a Committee on Public Affairs which became part of a new Division of Public Affairs when the proposed bylaws amendment was approved. This new Division also includes the Public Relations Committee, the Committee on National Legislation and the Committee on State Legislation. It is expected that this change will strengthen and co-ordinate the Society's activities in these areas. A large part of this Division's activities will be directed toward the members of the Society. The Public Affairs Committee will conduct a political education program for the members of the Society, thus allowing COMPAC to devote all its energies to political action. In these days when more and more of our professional activities are affected by legislation and the regulations promulgated by government agencies, it is important for all of us to become involved in the political process. Joining and participating in COMPAC is an important first step in this direction.

I need not tell you how the medical profession is besieged on all sides by its critics. Neither the Council nor the House of Delegates is omniscient. They need the help of an informed membership which participates actively in the affairs of Medicine at all levels so that its opinions can be heard and its wishes and decisions implemented. In these crucial times this need is greater than ever.

As your President I welcome whatever ideas and suggestions you have towards improving and strengthening the Society and making it more responsive to the membership and more relevant to the needs of the people of Connecticut. I am sure the Council and the House of Delegates join me in this regard.

Morris A. Granoff, M.D.

FROM THE EXECUTIVE DIRECTOR'S OFFICE

William R. Richards, M.D.
Executive Director

160 St. Ronan Street, New Haven, Conn. 06511
Telephone 865-0587

Josephine P. Lindquist
Associate Executive Director

SUMMARY OF ACTIONS COUNCIL MEETING

Wednesday, March 25, 1970

I. Attendance

Present in addition to the Chairman, Dr. S. J. Martin, and the Vice-Chairman, Dr. Kenneth F. Brandon, were: Drs. Granoff, Weber, Jr., Edson, Abbot, Dean, Gardner, Fabro, Polivy, Grendon, Rogol, Cramer, Harwood, Petrie, Wilson, Jr., Roch, Grant, Nemoitin, Friedberg, Johnson, McDonald, Gorin, Pelz, Root, Jr., vonGlahn and Klare.

Also present were: Mrs. Lindquist, Mr. Donelan (AMA), Dr. Hess, (Welfare Medical Director), Mr. Olson (Executive Secretary, FCMA) and Dr. Richards.

Absent were: Drs. Gallo, Purnell and Palomba.

II. Routine Business

Approval of Minutes

As printed and distributed, it was VOTED to approve the minutes of the meeting of February 19, 1970.

Life Membership

It was VOTED to approve an application for Life Membership received from the following eligible Active Member:

William V. Wener, Norwich (NLCMA)—1970

Dates of Meetings

The next regular meeting of the Council is scheduled to be held on Wednesday, April 29, 1970. A "special" meeting to receive and act upon the anticipated report of the Committee on Medical Economics and Insurance on Malpractice is tentatively scheduled to be held on Thursday, April 23, 1970, pending clearance by the Chairman with Dr. Deren and his attorney.

III. Old, New and Special Business

Election of Student Members

It was VOTED to elect to Student Membership the following residents of Connecticut who are attending medical schools in the United States:

David E. Peach, R.D. #1, Rockhouse Road,
West Redding
Yale University—1973
Pre-Med: Yale University
Parent: Edward T. Peach

Richard L. Sartini, 174 Parker Avenue, Meriden
Tufts University—1972
Pre-Med: College of Holy Cross
Parent: Salvio J. Sartini

Reports—Fiscal Advisory Committee

It was VOTED to act upon recommendations of the FAC as follows:

(a) *N.E. Council*: To authorize payment of 1970 dues in the amount of $150 to the Council of New England State Medical Societies.

As an adjunct to this action, it was further VOTED to accept the report of the Delegates to the CNESMS on continuing membership of the Society as follows:

(1) That payment of dues to CNESMS be made for 1970.

(2) That membership of the Society in CNESMS be continued at this time, and that any decision regarding a change in the membership status of CSMS be deferred until the structure and function of the N.E. Council have been discussed by the delegates of all states at that organization's next meeting.

(b) *Committee on Medical Economics and Insurance*: To authorize payment of a fee of $100 to Attorney Lorenzo H. D. Wildman, Bridgeport, for his attendance and participation in the "special" meeting of the Council at which the report on malpractice of the Committee is received and acted upon, provided that Dr. M. David Deren determines that the attorney's attendance and participation will be helpful to the Council in the consideration of the subject report.

(c) *United States Pharmacopeial Convention, Washington, D.C., April 8-10, 1970*: To authorize James E. O'Brien, Hartford, to attend this Convention as the official Delegate from CSMS, and to reimburse Dr. O'Brien for usual expenses incured thereby in the amount of up to $125.

Report—66th Annual Congress on Medical Education

It was voted to accept, with commendation, a report on the proceedings of this Congress (Chicago, 2/7-8/70) filed by Charles Polivy, Hartford, who attended as a representative of the Society. It was further VOTED to distribute informational copies of the report to members of the Committee on Postgraduate Education and of the Committee on Medical Education and Licensure (Connecticut Medical Examining Board).

Report—Ad Hoc Committee on Administrative Organization and Planning

The Council received a three-part report from this Committee and acted upon the three sections as follows:

(1) *Council Meeting Format*: After making several minor amendments, it was VOTED to approve a series of recommendations designed to "streamline" meetings of the Council, to expedite the work of the Council, and to allow the Council members more time to deal with substantive matters.

(2) *Applicants for Post of Assistant Executive Director*: It was VOTED to receive as information the report of the Committee that several applicants for this post are being evaluated, and that, following in-person interviews with members of the Committee, the Committee hopes to make a specific subject recommendation to the Council.

(3) *Additional Staff Personnel, etc.*: It was VOTED to approve the report and recommendations of the Committee with respect to "efforts to provide more definitive guidance to the leadership of the Society" so that representative efforts on behalf of the membership will become more effective, and with respect to the employment of additional "specialized" staff personnel as the need for same becomes evident to the leadership.

Communication—The Hartford County Medical Association

It was VOTED to receive a communication from the President of HCMA which proposed that the Council initiate the development of a "position paper" on medical and health care in Connecticut which would be responsive to four questions posed by a candidate for major elective office in the state, but would be made available to all candidates for major elective office as a possible medical and health care "plank" in their respective platforms. It was further VOTED to direct the Chairman of the Council to appoint an ad hoc committee to study, report and make recommendations on the matters outlined in the HCMA communication and a plan for implementing same by the Council, both assignments to be carried out with despatch.

Resolutions re Malpractice Study

(a) *From NHCMA*: It was VOTED to accept as information, and with thanks, a resolution adopted by the Board of Governors of NHCMA which urged "the Council and the Judicial Committee to proceed with all deliberate speed to resolve the malpractice crisis". The resolution was offered "as an indication of support for the efforts" of the Council and several CSMS committees to develop a positive program to alleviate the current problems associated with malpractice insurance coverage.

(b) *From LCMA*: It was VOTED to receive as information a resolution adopted by the Executive Committee of LCMA which called on CSMS, "Through appropriate channels, to study and search diligently for a solution to the crisis of professional liability" and to "study the feasibility of a CSMS malpractice insurance coverage plan, subscribed to and underwritten by CSMS Members". In accordance with the stated wishes of the LCMA Executive Committee, the resolution will be presented for discussion at the May meeting of the CSMS House of Delegates.

Resolution—Committee on Rural Health

Farm Tractor Overturn Protection: It was VOTED to approve a resolution on this subject, submitted by the Committee, and to refer to the Committee on State Legislation, for study and possible implementation, the question of sponsoring a bill at the 1971 General Assembly which would help to advance the purpose of the resolution; i.e., to encourage farm equipment manufacturers to develop and make available as standard equipment basic overturn protection for the operators of farm tractors and (legislatively) to make such protection a requirement for licensure of farm tractors.

Report—Committee on Third Party Payments

(a) *Addition to Previous Report on HCMA Proposal for Insurance-Prepayment Plan*: It was VOTED to approve, and make an integral part of the previous subject report, a new paragraph (e), under Section (3)—Criteria for Foundation Endorsement", to read: "Agreement by all third party payors operating Foundation-endorsed programs to make benefits payments directly to physicians having participation agreements with the Foundation". All County Medical Associations (to which the previous report was sent) are to be apprised of this approved amendment to the report.

(b) *Prompt Payment of Claims*: It was VOTED to approve a policy statement, submitted by the Committee, and to apprise the CSMS Liaison Committee with CG on Medicare B of this action. The statement read: "All payments by responsible third party payors should be made within thirty (30) days of the receipt of properly completed claim forms".

Connecticut Regional Medical Program

(a) *Report on CUPISS*: It was VOTED to table action on this progress report, which was submitted by Isadore H. Friedberg, Newington, CSMS representative on the CUPISS Technical Advisory Committee (CRMP). It was further VOTED to request the Chairman to appoint an ad hoc committee of three members of the Council who are members of the Judicial Committee to inquire of the Meriden Hospital how, in processing CUPISS in-put information, it is protecting the confidentiality of patients and how it is handling "informed consent", and to report its findings to the Council. The Chairman appointed the following:

J. Alfred Fabro, Torrington, Chairman
Clarence W. Harwood, Middletown
Regionald C. Edson, West Hartford

(b) *Reports on CRMP Activities*: It was VOTED to receive as information a series of verbal reports made by Drs. Gardner, Martin, Abbot and Johnson (CSMS designates on CRMP Advisory Board), Drs. Polivy, Petrie, Friedberg, Cramer, Grendon, Richards and others. In summary, it appeared to be the consensus of opinion among the Council members that these reports, in toto, did not paint a very clear picture of what CRMP is currently doing, or not doing, in a variety of areas of program planning and/or implementation. Pursuant to a lengthy discussion of these matters, two actions were taken as follows:

(1) *Appointment of Ad Hoc Committee*: It was VOTED to direct the Chairman to appoint an Ad Hoc Committee, composed of Drs. Abbot, Rogol, Johnson, Edson and others, (Granoff), to undertake the following studies, with subsequent report to the Council:

(A) A review of current CRMP activities in all areas of program planning and implementation.

(B) The provisions and significance of a bill (S. 3443—91st Congress), introduced by Senator Javits (N.Y.) which is reported to call for the merger of Regional Medical Programs and Comprehensive Health Services and Resources Planning with a view to eliminating areas of duplicative activities and making more effective the non-duplicative activities of each.

(2) *Instruction to CSMS-Designates on CRMP Advisory Board*: It was VOTED to instruct the CSMS-designates serving on the CRMP Advisory Board to protest (a) the paucity of CRMP programs directed to patient care, and (b), the use of grant funds to increase CRMP public relations and publicity and for expanding the staff.

Reports—Committee on Accident Prevention

(a) *Responsibility of Attending Physician at Athletic Contests*: It was VOTED to approve a policy statement, developed by the Committee and approved by the Connecticut Interscholastic Athletic Conference, which defines the responsibilities and authority of a physician in official attendance at athletic contests with respect to determining the physical fitness of a player to continue participation in a game. It was further VOTED to approve the recommendation of the Committee that this policy statement be publicized to the membership in the Journal.

(b) *Proposed System of "Flagging" Passing Physician at Accident Scene*: It was VOTED to approve, in principle, a proposed system of indicating to physicians passing the scene of an accident that attendance of injured persons is needed by having highway patrolmen affix colored pennants to the radio antennas of their cars or motocycles. It was further VOTED to refer back to the Committee, for study and report, the following matters relating to the proposed system:

(1) Discuss with the State Police authorities possible practical alternatives to the pennant system proposed; i.e., some simpler means of giving notice to the passing physician which would not require special equipment.

(2) Determine how many pennants would be needed to effectively implement the proposal, and how they would be distributed to the patrolling officials.

(3) Based on the findings of (2), and with CSMS staff assistance, obtain cost estimates for the production and distribution of the proposed pennants, such estimates to be submitted to the Council with a request for approval.

(c) *Training for Ambulance Drivers and Attendants*: It was VOTED to approve a policy statement, recommended by the Committee, that "all ambulance drivers and attendants should have a minimum of training equivalent to the Red Cross Advanced First Aid Course". It was further VOTED to apprise a member of the State Ambulance Commission, Harold S. Barrett, M.D., of this action.

Report—Committee on Investment of Funds

It was VOTED to approve the recommendations of the Committee that the Second National Bank, New Haven, be retained as the Society's investment counsellor, and that the funds continue to be invested "prudently" in accordance with the advice of the counsellor.

Proposed FDA Brochure re Oral Contraceptives

It was VOTED to receive as information, and with thanks, a communication from the president of the California Medical Association regarding the inappropriateness and possible medico-legal hazards of a brochure drafted by the Food and Drug Administration which FDA proposed to require be distributed with all prescriptions for oral contraceptives prescribed by physicians and dispensed by pharmacists. In light of reports that, in response to criticisms from many sources, FDA has withdrawn its draft and is currently preparing a more acceptable one, no further action was taken in this regard. When the text of the new draft becomes available, it will be reviewed as to content and professional acceptibility.

Resolution re Standard Insurance Forms

A resolution submitted by the Executive Committee of the Litchfield County Association requested that the Council undertake a study of the feasibility of "standard" insurance forms. Noting that the House of Delegates (12/11/69) had not adopted a similar resolution (from LCMA), on the grounds that it is not feasible to try to insist that all third party payors agree to accepting standard forms and that standard forms are already available for use with third party payors who will accept them, the Council VOTED to advise the Executive Committee of LCMA that, if desired, the resolution can be resubmitted to the House of Delegates for consideration at the Annual Meeting in May.

N.B.: *The foregoing is a summary of the proceedings and action of the Council on March 25, 1970. Detailed minutes of the meeting are on file at 160 St. Ronan Street, New Haven, for perusal by any interested member of the Society.*

Placement Wanted

GENERAL PRACTITIONER — 32 years of age wishes emergency room position in Connecticut. Presently in practice. Military obligations completed. Connecticut license in process.

PATHOLOGIST—39 years of age with Connecticut license seeking directorship of laboratory of similar position. Has eight years experience as laboratory director. Available when right position arises.

UROLOGIST—31 years of age with National Boards wishes group or associate type practice in Connecticut. Military obligation completed.

PHYSICIAN—43 years of age interested in emergency room or as a house physician in the Fairfield area. Eligible with National Boards. Available immediately.

INTERNIST—30 years of age with National Boards wishes associate type practice in Connecticut. Military obligation completed.

OB & GYN—30 years of age. Eligible with National Boards wishes group or associate type practice in Connecticut. Available in July when military obligation completed.

INTERNIST—35 years of age wishes group or associate type practice in Connecticut. Eligible with National Boards. Presently in practice as chief of medicine. Available in July when military obligation completed.

UROLOGIST—31 years of age wishes group or associate type practice in Connecticut. Eligible. Military obligation completed.

DERMATOLOGIST—30 years of age wishes solo, group or associate type practice in the Fairfield County area. Certified with National Boards. Presently in practice. Available when military obligation completed in July.

GENERAL SURGERY—33 years of age wishes group or associate type practice in Connecticut. Certified with National Boards. Available when military obligation completed in July.

INTERNIST—31 years of age wishes to practice in Connecticut. Available upon request.

RADIOLOGIST—34 years of age wishes group or associate type practice in Connecticut. Eligible with National Boards. Military obligation completed.

OPHTHALMOLOGIST—31 years of age wishes group or associate type practice in Connecticut.

Eligible with National Boards. Presently in practice. Available when military obligation completed in July.

DERMATOLOGIST—35 years of age wishes group type practice in Connecticut. Presently in practice. Certified. Available in July.

ORTHOPEDICS—31 years of age wishes group or associate type practice in Connecticut. Eligible. Available in July.

RADIOLOGIST—31 years of age wishes group or associate type practice in Connecticut. Eligible with National Boards. Available when military obligation completed in June.

INTERNIST—31 years of age wishes group or associate type practice in Connecticut. Eligible with National Boards. While serving in the Air Force he held positions as Chief of Medicine and Chief of Hospitals. Presently in practice. Available when military obligation completed in July.

MEDICAL DIRECTOR—54 years of age wishes institutional type practice in Connecticut. Eligible. Presently in practice. Connecticut license.

NEUROLOGIST—30 years of age, Eligible with National Boards wishes group or associate type practice in Connecticut. Would prefer practice in a multispecialty group preferable with another neurologist.

INTERNIST—30 years of age, Eligible with National Boards wishes solo, group or associate type practice in the south west part of Connecticut. Would consider part or full time hospital practice with some subspecialty work in renal or dialysis medicine. Military obligation will be completed in July, available then.

UROLOGIST—52 years of age, Certified, wishes solo or group type practice in Connecticut. Available immediately.

PATHOLOGIST—34 years of age, Certified with National Boards, wishes associate type practice in Connecticut. Presently in practice.

OB & GYN—32 years of age, Eligible, wishes solo, group or associate type practice in Connecticut. Presently in practice, with Connecticut license.

UROLOGIST—32 years of age, with National Boards, wishes group or associate type practice in Connecticut. Would prefer to go in with at least one other man fairly near a good size hospital. Presently in practice.

PSYCHIATRIST—38 years of age, Eligible with National Boards wishes to practice in Connecticut. Presently in practice. Has done a good deal of in-patient and out-patient work.

INTERNIST-ALLERGY—31 years of age, Certified, with National Boards, wishes group or associate type practice in Connecticut. Presently in practice with Connecticut license. Military obligation completed.

PREVENTIVE MEDICINE—35 years of age, wishes institutional or industrial type practice in Connecticut. Presently in practice with Connecticut license. Available immediately.

INTERNIST—32 years of age, Eligible with National Boards, wishes solo type practice in Connecticut. Presently in practice with Connecticut license.

ANESTHESIOLOGY—38 years of age, Certified, wishes group or associate type practice in Connecticut. Presently in practice with Connecticut license. Military obligation completed. Available immediately.

SURGEON—35 years of age, Certified, wishes group, associate or institutional type practice in Connecticut. Presently in practice with Connecticut license. Military obligation completed. Available immediately.

PEDIATRICS—31 years of age, Eligible with National Boards, wishes group type practice in Connecticut. Group practice at large teaching hospital or university hospital preferred.

GENERAL PRACTICE OR PEDIATRICS—32 years of age wishes part-time position for the month of July.

INTERNIST—31 years of age, Eligible with National Boards, wishes solo, group or associate type practice in Connecticut. Interested in the area along the southern coast of Connecticut between 40 and 120 miles from New York City.

PHYSICAL MEDICINE AND REHABILITATION-ELECTRO NEUROMYOGRAPHY DIAGNOSIS—44 years of age, Board eligible, wishes group, associate or full time institution practice. Available mid-summer.

ANATOMIC PATHOLOGY—38 years of age, Certified, wishes to practice in Connecticut. Military obligation completed. Available immediately.

ANESTHESIOLOGY—56 years of age, Certified, wishes group, associate, institutional or industrial type practice in Connecticut. Available immediately.

PHYSICIAN-COLLEGE HEALTH — 26 years of age, with National Boards, wishes group or associate type practice in Connecticut.

OB & GYN—37 years of age, Certified, wishes associate or group type practice in Connecticut. Presently in practice with Connecticut license.

PHYSICIAN—26 years of age, wishes group type practice in Connecticut. Available mid-summer.

INTERNIST—32 years of age, Eligible with National Boards, wishes group or associate type practice in Connecticut. Seeking a position in internal medicine with an emphasis on chest disease preferably associated with a hospital where he can provide pulmonary function testing and good respiratory care.

ANATOMIC & CLINICAL PATHOLOGY — 31 years of age, Eligible with National Boards, wishes solo or associate type practice in Connecticut. Military obligation completed.

SURGEON—32 years of age, Eligible with National Boards, wishes solo, group or associate type practice in Connecticut.

INTERNAL MEDICINE-GASTROENTEROLOGY—31 years of age, Eligible with National Boards, wishes group or associate type practice in Connecticut.

PEDIATRICIAN—30 years of age, Board Eligible with Connecticut license. Desires associate type practice in Connecticut leading to partnership with another pediatrician or group practice.

INTERNIST—38 years of age, Certified with National Boards, wishes solo or associate type practice in Connecticut. Presently in practice. Military obligation completed. Available immediately.

ANESTHESIOLOGIST—36 years of age, Certified, wishes group, associate or institutional type practice in Connecticut. Seeking position where he could use his experience in respiratory care and anesthesia for cardio-pulmonary surgery. Presently in practice.

UROLOGIST—34 years of age, Certified, wishes group or associate type practice in Connecticut. Presently in practice.

OBSTETRICS AND GYNECOLOGY—35 years of age, Eligible with Connecticut license, wishes group, associate or institutional type practice in Connecticut.

ANYONE INTERESTED IN THE ABOVE IS ASKED TO CONTACT THE PHYSICIANS PLACEMENT SERVICE, 160 ST. RONAN STREET, NEW HAVEN, CONNECTICUT 06511.

Placement Opportunities

GENERALIST OR INTERNIST—Growing central Connecticut residential community, fine schools, quiet country living. Twelve miles from 400 bed general hospital. For further information write or call William B. Lyons, M.D., R.D. #2, Kettletown Road, Southbury, Conn. 06488, Tele. 264-8884.

CAMP PHYSICIAN—for approximately 300 summer campers (boys and girls) at Winchester Center, Connecticut. 8 weeks period, beginning late June, 1970; would accept two physicians for consecutive four-week periods. Two R.N.'s in resident attendance. Salary open. Requirements: Must have Connecticut License; may be intern, resident, in practice or retired; with or without family.

MEDICAL DIRECTOR—40 hour week! All holidays! Regular vacations! No nights! All staff and equipment paid for by company. In short a high level professional staff position for a General Practitioner or Internist with a leading industrial firm in North Central Connecticut. Industrial experience not required but even part time exposure would be a plus. Will deal with various industrial health and safety problems and supervise a staff of five. Solid, well run firm. Excellent benefit program. Fine opportunity to grow. Starting salary $25,000. Naturally, all fees are paid by the client company. For completely confidential interview send curriculum vitae or call UNI/SEARCH, 15 Lewis Street, Hartford, Connecticut; 278-8040.

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JOURNAL

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Electrocardiogram of the Month

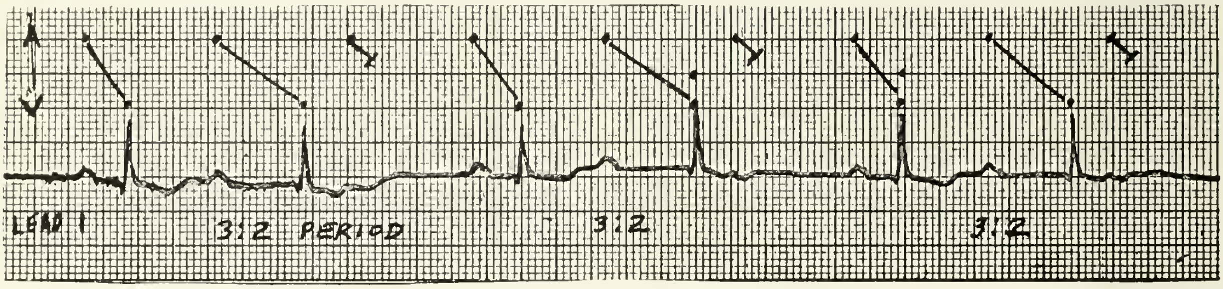
Yale-New Haven Hospital
New Haven, Connecticut

Prepared by
HYMAN M. CHERNOFF, M.D.
Associate Professor of Clinical Medicine,
Yale School of Medicine
Director, Dept. of Electrocardiography
Memorial Unit, Yale-New Haven Hospital

One of the common manifestations of digitalis excess is the occurrence of impaired conduction through the A-V junctional tissues. This may take the form of mere prolongation of the PR interval without the dropping of a ventricular beat (first degree A-V block), and is, therefore, easily recognizable in the electrocardiogram. More advanced intoxication with digitalis often produces a type of 2nd degree A-V block in which there is progressive prolongation of the PR interval until an atrial beat is completely blocked resulting in a dropped ventricular beat, and following this pause the next atrial beat is again conducted to the ventricle and the sequence may keep repeating itself. This has been referred to as the Wenkebach phenomenon and the term Wenkebach period is used to denote the ratio of atrial to ventricular beats in each such sequence. This ratio may be constant or may keep changing in a given patient. The recognition of the presence of this phenomenon in the electrocardiogram is, therefore, of great import to the physician who is prescribing digitalis. Usually this is without any particular difficulty. At times, however, the diagnosis is more obscure, especially when *all* the atrial beats (P-waves) are not easily recognizable in the tracing, particularly when they may be buried in the QRS complexes or superimposed on the ST-T segments.

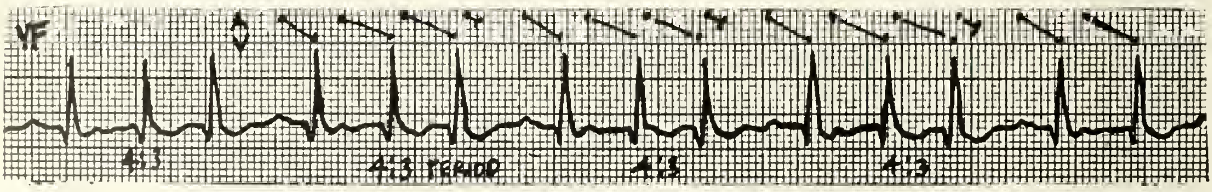
Below are several examples of the Wenkebach phenomenon in which the diagnosis of the phenomenon may at first glance not be obvious to everyone. The grouping of ventricular beats should raise the suspicion of the presence of the phenomenon and the technique of ladder-diagramming as shown below is useful in demonstrating it beyond any doubt.

A



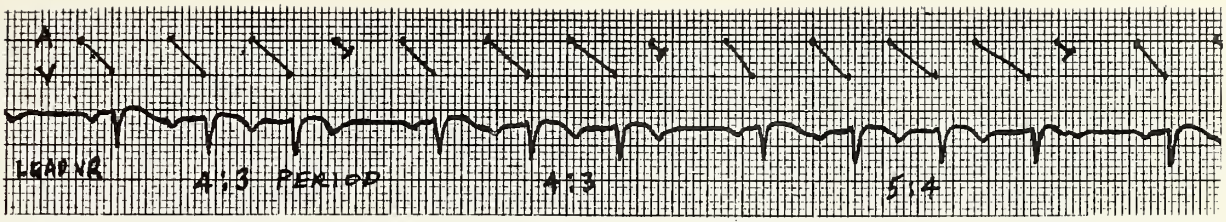
A—The ventricular beats are grouped in pairs due to successive 3:2 Wenkebach periods. The atria are beating at 80 per minute. The PR interval of the first beat of each sequence measures 0.24 sec. It then lengthens to 0.50 sec. The next P-wave is completely blocked and then the sequence repeats itself. The blocked P-waves can be seen superimposed on the ST segment of the preceding ventricular complex.

B



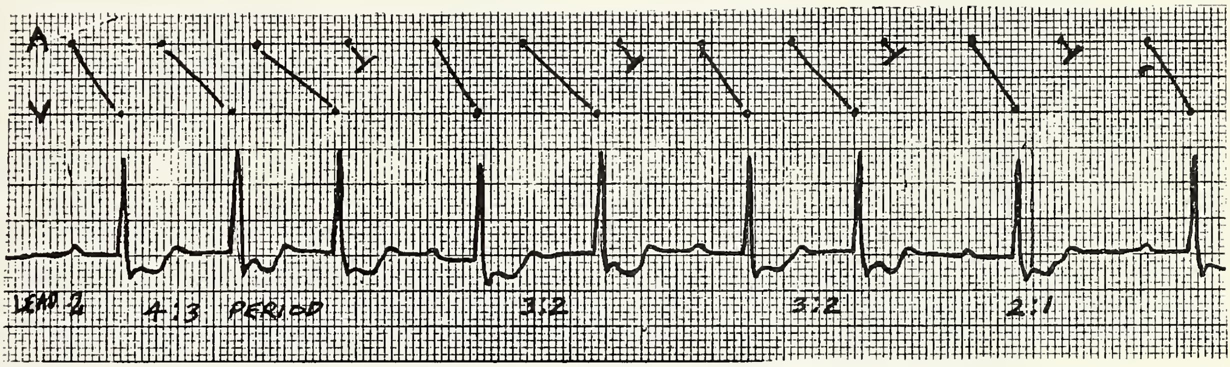
B—The ventricular beats are grouped in trios due to successive 4:3 Wenkebach periods. The atria are beating at about 166 per minute. The PR interval of the first beat of each sequence measures about 0.20 sec. The next PR interval measures 0.26 sec. The 3rd PR interval measures 0.28 sec. The next P-Wave is completely blocked and then the sequence repeats itself. The second P-wave of each sequence is superimposed on the ST segment of the preceding ventricular complex. The third and fourth P-waves are merged with the QRS complex and thus are not readily identifiable.

C



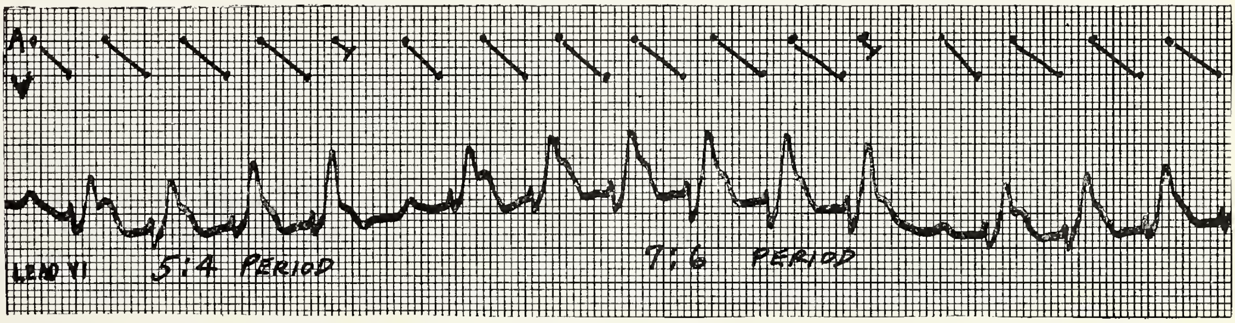
C—There are two successive 4:3 Wenkebach periods followed by a 5:4 period. The atrial rate is 130 per minute. The PR interval of the first beat in each sequence measures about 0.16 sec. It progressively lengthens until a P-wave is completely blocked. Some of the sinus P-waves in this lead VR may be mistaken for inverted T-waves when they fall at the end of a ventricular complex. In this patient the T-waves are actually low upright as noted in the first beat of each sequence.

D



D—There is a 4:3 Wenkebach period followed by two successive 3:2 periods and then a 2:1 period. The atria are beating at about 115 per minute. The PR interval of the first beat in each sequence measures about 0.26 sec. The PR interval progressively lengthens until a P-wave is completely blocked. A prominent upright U-wave follows the inverted T-waves of each ventricular complex and should not be mistaken for an upright P-wave. The second P-wave in each sequence is superimposed on the terminal upstroke of the T-wave. The third P-wave in each sequence is superimposed on the initial portion of the ST segment. The fourth P-wave (in the 4:3 period) is buried in the QRS complex and is therefore not visible.

E



E—There is a 5:4 Wenkebach period followed by a 7:6 period. The atrial rate is about 136 per minute. The PR interval of the first beat in each sequence measures about 0.24 sec. The P-waves of the succeeding beats are at first superimposed on the initial portion of the ST segments and then are merged with the abnormally wide QRS complexes and are therefore not visible.

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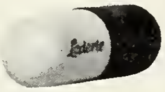

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By The London Post

British National Health Services

Part V

Ned Thomas

(This is the fifth of a series of six articles).

"More persons are getting better medical attention than they did prior to 1948 when the National Health Service was established."

"The medical care that the majority of people are getting under the National Health Service is definitely improved over what it was before it."

These opinions were spoken by two National Health Service doctors at different times and at different places. Unknown to one another, both doctors reflected the same basic view. Their view is typical of many physicians in the health service.

The first statement was made by a general practitioner who practices medicine solo in the industrial Midlands of England and who prefers to remain anonymous. The second statement was spoken by Dr. Anthony Dunnill, a G.P. who is in partnership with three other doctors at the East Oxford Health Center, near Oxford University.

Dr. Dunnill said, "People who formerly didn't see doctors due to their inability to pay for it are now able to see them. Consequently, more people are getting more medical care."

Although both doctors have some reservations about the National Health Service, neither one would want to leave it and return to private practice.

Dr. Dunnill asserted that the National Health Service is "working out very well for me. I'm quite happy to be part of it." He said he felt this way because of a new pay structure for doctors and the improvement of conditions, such as the building of new health centers. He works in a modern, well equipped, up-to-date clinic.

The Midlands doctor is also satisfied with his lot. "As a doctor," he said, "I feel that the National Health Service is good for me." He added that he is looking forward to retirement and that he will receive a pension from the National Health Service. It will enable him and his wife to live "in reasonable comfort," he said.

Dr. Dunnill likes the aspect of the National Health Service that provides free, comprehensive medical and health care to everyone, regardless of their financial condition. He said:

"I do not think that people should have to think of finances when they are ill and need medical attention. Furthermore, I do not like to consider a patient's financial condition when I treat him."

Dr. Dunnill said it was his opinion that the health of the people of England is not suffering because of the way that the National Health Service is now constituted.

"The patients," he said, "seem to be very satisfied with the National Health Service."

On the critical side, Dr. Dunnill said, "The situation is very poor in the hospitals. Doctors are overworked and underpaid. Therefore, a lot of them are emigrating to Australia, Canada and the U.S.

"They are being replaced by immigrant doctors from the West Indies, India and Pakistan. These doctors are prepared to work hard for less pay in order to earn a post-graduate degree, after which they want to return to their native lands and earn big money."

This situation, Dr. Dunnill added, is causing a constant turnover of less experienced doctors. He said that hospital doctors should be paid more money according to their work load, number of hours they work and their responsibility.

The Midlands doctor thinks the National Health Service is "a good thing in theory. But in practice," he said, "it's abused by the hypochondriac and the malingerer. The result is that quite a number of those who may be in need of medical attention aren't able to avail themselves of the medical facilities. The hypochrondriacs and malingerers are the bane of our lives."

"If some deterrent could be introduced to prevent the hypochondriac and malingerer from monopolizing the doctor's time," the Midlands doctor said, "the individual, who is genuinely in need of medical attention, would find it more readily available to him."

MR. NED THOMAS is a science medical writer for the New Haven Register on leave.

He said he works long hours and sees about 60 patients a day, five days a week. He also works half days on Saturdays and is on duty every third night, but he said he doesn't feel overworked. He added that he worked as hard when he was in private practice.

The Midlands doctor thinks that while doctors generally fare well under the National Health Service, patients do not fare as well as they might under a free system.

He said that patients who need specialized care may have to wait for months and sometimes for years if their conditions do not demand urgent and immediate attention of specialists.

However, he pointed out that patients in urgent need of medical attention by specialists receive "speedy and excellent attention." He noted that patients who have less urgent medical conditions may have to see specialist doctors on a private basis for correction of such ailments as varicose veins or an uncomplicated hernia.

While he said that most patients are "reasonably satisfied" with the National Health Service, he observed that most of the dissatisfaction expressed to him by patients is directed at the bottleneck in seeing specialists.

Dr. Dunnill echoed this complaint. He said he would like to see "a closer liaison between specialists and G.P.s. He said that he also favors better access to laboratories and would like to see a system set up to help patients who need it to get to the clinic.

Admitting that American doctors are better off financially than British doctors, Dr. Dunnill said, "but then the cost of living is higher in America. I also think that doctors in the U.S. work harder than we do and are on call all of the time."

The Midlands doctor declared that as a private physician he had to be "more self-reliant" in making diagnoses of patients' ailments than he does as a National Health Service doctor. Currently, he refers many patients to specialists for diagnosis.

He no longer has to consider the patient's pocketbook, he said, before referring a patient to a specialist. Under the National Health Service it doesn't cost the patient any money to be referred to one. "However," he noted, "it takes more of the patient's time and perhaps delays treatment."

"But when the patient is finally seen by the specialist, the treatment is first class," he added. In the overall picture, however, he noted that patients are not neglected, even with delays in the consultant system.

(The sixth report in the series discusses the brain drain in England, as regards the National Health Service.)

Members of the Connecticut State Medical Society reading papers before other organizations are requested to submit their papers to the JOURNAL for consideration by the Board of Editors for publication. Please send them to:

Louis H. Nahum, M.D., *Editor*
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LAW—MEDICINE NOTES

J. Alfred Fabro, M.D.

BRUNE v. BELINKOFF

This case involves the legal standard of care required of a physician. The question: Is it to be determined on a purely local basis, or regional, or state, or national?

The legal principle has been that the standard required of the physician is set by his medical colleagues and not by the ordinary or lay person. Also, the standard required has been that of physicians practicing in his community, on the grounds that it would be unfair to require a rural practitioner to have the equipment, facilities and experience of a physician practicing in urban or university settings.

The standard required varies from state to state. As shown in this case, it is set not by the legislatures in statutory form, but by decisions of judges in the tradition of the common law-judge-made, case by case, state by state.

Therefore, the physician must understand that the legal standard required of him in his practice varies from state to state. He must look to his own state for the legal standard—usually not in the written laws (statute), but in court decisions. This recent case in Massachusetts demonstrates the method and reasoning in which the law was changed there—by its highest court.

Some states have set the standard as that of the locality or community. The difficulty arises as to definition. What is the geographic extent of the locality or community?

Another group of states defines the standard as "the same or similar" communities. This also presents the problem: The same or similar in what way? Socio-economically or medically, for example?

A third group applies the so-called "similar circumstances" doctrine. The locality is but one of the circumstances to be considered in determining the standard to be used.

Also added is the applicable case in Connecticut as expressed by our Supreme Court of Errors.

In 1968 the Supreme Judicial Court of Massachusetts, in overruling a lower court, upset an important legal precedent, and established another—for Massachusetts.

It held that the conduct of a specialist, an anesthesiologist, was measurable not by the skill and ability of physicians in a city of 100,000 (New Bedford), slightly more than 50 miles from one of the medical centers of the nation (Boston), but by the skill of the average member of the profession practicing the specialty, taking into account the advances in the profession and medical facilities available.

The precedent had been established in 1880 in a case in which a general practitioner in a town of 2,500 treated a patient with a severe wound requiring a "considerable degree of surgical skill."

In this suit, the issue was "How much skill or what standard does the law require of the defendant physician?" That judge instructed the jury, in its determination of whether or not he was negligent, that "A physician in a small country village does not usually make a specialty of surgery, and however well informed he may be in the theory of all parts of his profession, he would, generally speaking, be seldom called upon as a surgeon to perform difficult operations. . . . He was bound to possess that skill only which physicians and surgeons of ordinary ability and skill, practicing in similar localities, with opportunities for no larger experience, ordinarily possess; and he was not bound to possess that high degree of art and skill possessed by eminent surgeons practicing in large cities, and making a specialty of surgery." This was called the "community" or "locality" rule.

In the recent New Bedford case the facts were: The patient-plaintiff was delivered of a baby in a local hospital. The defendant, a specialist in anesthesiology, gave her a spinal anesthetic containing 8 milligrams of Pontocaine and 10% glucose solution. Eleven hours later the patient in trying to get out of bed slipped and fell. She developed numbness and weakness in her left leg that has persisted.

Eight physicians testified as expert witnesses. Some that "there was ample evidence that her condition resulted from an excessive dosage of Pontocaine"; and "good medical practice required a dosage of 5 milligrams or less." Testimony by these physicians was, as usual, conflicting.

The dose of 8 milligrams was customary in New Bedford, but was 5 milligrams in Boston. The de-

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DR. J. ALFRED FABRO, senior attending surgical staff of the Charlotte Hungerford Hospital, Torrington, Conn.

fendant testified that the differences in dosages were due to differences in obstetrical technique in the areas. Local obstetricians used suprafundal pressure so that more and higher anesthesia was required.

In instructing the jury as to the legal standard required of the anesthesiologist, the judge stated, "[he] must measure up to the standard of professional care and skill ordinarily possessed by others in his profession in the community, which is New Bedford, and its environs . . . where he practices, having regard to the current state of advances of the profession. If, in a given case, it were determined by a jury that the ability and skill of the physician in New Bedford were 50% inferior to that which existed in Boston, a defendant in New Bedford would be required to measure up to the standard of skill and competence and ability that is ordinarily found by physicians in New Bedford." This instruction by the trial judge followed the prevailing law in the state—the standard required is determined by that of physicians practicing in the same community or locality.

The jury found for the doctor. Plaintiff appealed on the ground that the judge had incorrectly instructed the jury as to the standard required of the doctor—that of an anesthesiologist practicing in New Bedford, even if "50% inferior to that which existed in Boston."

The issue for the highest court was "whether the defendant was to be judged by the standards of doctors practicing in New Bedford."

The court stated "The degree of care which must be observed is, of course, that of an average competent practitioner acting in the same or similar circumstances. In other words, local practice within geographical proximity is one, but not the only factor to be considered. No longer is it proper to limit the definition of the standard of care which a medical doctor or dentist must meet solely to the practice or custom of a particular locality, a similar locality or a geographic area." Rapid methods of transportation and easy means of communication have changed the standards of practice. American Boards also tend to make the standards national, not local.

The court concluded, "We are of the opinion that the 'locality' rule . . . which measures a physician's conduct by the standards of other doctors in similar circumstances is unsuited to present day conditions. The time has come when the medical profession should no longer be Balkanized by the application of varying geographic standards in malpractice. Accordingly, Small v. Howard is overruled. The proper standard is whether the physician, if a general practitioner, has exercised the degree of care and skill of the average qualified practitioner, taking into account the advances in the profession. In applying this standard it is permissible to consider the medical resources available to the physician as one circumstance in determining the skill and care required. Under this standard some allowance is thus made for the type of community in which the physician carries on his practice.

"One holding himself out as a specialist should be held to the standard of care and skill of the average member of the profession practicing the specialty, taking into account the advances in the profession. And, as in the case of the general practitioner, it is permissible to consider the medical resources available to him."

This decision becomes in effect the law in Massachusetts as to the standards of skill required of physicians. It is no longer based on the locality. It remains, however, one of the factors to be considered.

GERATY v. KAUFMAN

In its opinion, the Massachusetts court quoted with approval the standard of care required of physicians in Connecticut as established by its highest court, the Supreme Court of Errors, in 1932.

In this case, the patient suffered a fracture of both bones of his left leg. The doctor, a physician and surgeon, reduced the fracture and applied a circular plastic cast. Impairment of circulation developed. The cast was bivalved and removed, but ulceration and sloughing of the tissues occurred resulting in shortening of the leg and permanent lameness.

There was the usual conflicting testimony of physicians testifying as experts as to the proper care and the standard of care required. Those testifying for the patient stated that the standard of care followed by the physician did not accord with the standard followed throughout the state. Defendant physician offered evidence that he had followed practice in New London and in other parts of the state.

The plaintiff produced a surgeon who testified that he specialized in orthopedic surgery, that he had charge of the fracture work in a hospital in Bridgeport for 8 years, and had done fracture work in hospitals in Milford, Derby, and New Haven. He was asked if he knew the usual custom of physicians and surgeons in the general neighborhood of Connecticut in a matter of application of plaster casts and replied in the negative. Defendant objected that this surgeon was not familiar with the standards of care in New London. The trial judge, however, ruled that he could testify, reasons given below.

To the court, the test, in determining "what constitutes reasonable care, skill, and diligence, is that which physicians and surgeons in the same general neighborhood and in the same general line of practice ordinarily have and exercise in like cases." The judge could have as a matter of law ruled that this surgeon could not testify as an expert to the standards in the general area of New London, but he stated that "it was for the jury [after hearing the evidence] to say whether New Haven and New London were in the same general neighborhood from a medical standpoint."

He stated that "a country surgeon should not be expected to exercise the high degree of skill possessed by eminent surgeons living in large cities and making a specialty of surgical operations. For this reason it is generally held that some reasonable territorial limitation should be fixed in determining the standard of comparison, and in some jurisdictions it has been held to be that of physicians and surgeons in 'the same neighborhood,' or 'the same locality.' A rule does not restrict the territorial limitation to the confines of the town or city in which the treatment was rendered, and under modern conditions there is perhaps less reason than formerly for such restriction. There is now no lack of opportunity for the physician or surgeon in smaller communities to keep abreast of the advances made in his profession, and to be familiar with the latest methods and practices adopted. It is not unreasonable to require that he have and exercise the skill of physicians and surgeons in similar localities in the same general neighborhood. It may not be sufficient if he exercises only that degree of skill possessed by other practitioners in the community in which he lives."

The defendant objected to this instruction to the jury. He appealed that his handling of the case should be judged on the standards of his own local community and the area, and not beyond that, as in New Haven. The issue revolved around whether the expert should have been able to testify as to the standard of practice in communities other than in New London.

The Supreme Court, in holding that he could, stated, "We think that a surgeon may properly be permitted to testify as to the general practice in the state in the application and treatment of plaster casts. It may fairly be assumed that the standard practice in such a matter would not materially differ in the various hospitals in the state and in fact there was evidence in the case that this was true. There is no unfairness to the defendant in admitting such evidence, and a case might well arise in which it would be a practical impossibility for the plaintiff to procure expert witnesses who could testify that they know what the practice was as to a particular operation in a particular community."

Therefore, the rule does not restrict territorial limitation to the confines of the town or city in which the treatment is given. Under modern conditions there is less reason for such a rule than formerly. The jury determines whether a defendant acts in accordance with practice in the same general neighborhood with the implication that it is within the province of the jury to determine the extent of the general neighborhood. Connecticut is geographically a small and compact state. There is the implication of Connecticut decisions that the general neighborhood is the state of Connecticut.

NEW BOOKS RECEIVED

Books received for review are acknowledged in this department and such acknowledgement must be regarded as a sufficient return for the courtesy of the sender. Selection will be made for review in the interests of our readers and as space permits. Books are listed with advance data supplied by publishers. Prices quoted are not guaranteed. For further information, address queries to the publishers.

Cardiovascular Surgery Current practice, Volume 1. Edited by Thomas H. Burford, M.D., Professor of Clinical Thoracic and Cardiovascular Surgery, Washington University School of Medicine; Associate Thoracic Surgeon, Barnes Hospital and Saint Louis Children's Hospital, Saint Louis, Missouri and Thomas B. Ferguson, M.D., Associate Professor of Clinical Thoracic and Cardiovascular Surgery, Washington University School of Medicine; Attending Thoracic Surgeon, Barnes Hospital and Saint Louis Children's Hospital, Saint Louis, Missouri. The C. V. Mosby Co., St. Louis, Missouri. With 134 illustrations. 273 pp. $18.00.

Mastering Your Emotions—Mental Health Through the Reeducation of Self. Edited by William B. Terhune, M.D., Medical Director Emeritus, Silver Hill Foundation, New Canaan, Connecticut. William Morrow & Company, Inc., New York, 1970. 249 pp. $5.95.

From the

Connecticut Regional Medical Program

Henry T. Clark Jr., M.D., Director

This column launches a series of monthly letters which seek to familiarize the medical profession of Connecticut with the workings of the Connecticut Regional Medical Program (CRMP). In future columns the details of specific program activities—and their potential benefits to practicing physicians and the patients they serve—will be related.

Readers of the *Journal* will recall a discussion of CRMP in these pages on three previous occasions. The first appeared in a September, 1966 article by Arthur Ebbert Jr., M.D., Associate Dean of the Yale University School of Medicine, entitled "A Look at Public Law 89-239: The Heart Disease, Cancer, and Stroke Program." It reviewed the need for and the provisions of the legislation and listed the steps taken up to that time to implement the law in Connecticut.

"The Connecticut Regional Medical Program and the Family Physician" (September, 1968), told of the need to encourage, through local initiative, better teamwork among the various elements of the health care system in Connecticut in the interest of good patient care.

In February, 1969 a comprehensive review of the program, its guiding philosophy, and emerging operational activities were presented in the article, "Connecticut Regional Medical Program – From Planning to Operations."

Nevertheless, it may be useful in this initial column to retrace our steps and cite pertinent sections of P.L. 89-239, the regional medical program legislation, and explain how we in Connecticut have interpreted the law to develop the kind of program we now have. Through such understanding may come better physician appreciation of the potential the program offers all of us to achieve dramatic gains in the quality and scope of health care available to Connecticut's three million citizens.

Law Purpose Stated

The law states that its purpose is: "to encourage and assist in the establishment of regional cooperative arrangements among medical schools, research institutions, and hospitals for research and training (including continuing education) and for related demonstrations of patient care in the fields of heart disease, cancer, stroke and related diseases."

Equally important, from the patient's standpoint, is that P.L. 89-239 affords the medical profession and medical institutions (again quoting the law), "through such cooperative arrangements, the opportunity of making available to their patients the latest advances in the diagnoses and treatment of these diseases." This reflects a shift in the attitude of Congress from its historic emphasis on supporting basic research to a concern for patient care. Regional medical programs, Congress declared, would bridge the gap between the centers of excellence where so much valuable research was going on and the "people back home"—the physicians and the patients who would benefit from the fruits of this new knowledge. It would be a catalytic agent to facilitate changes in the health care delivery system, responding to the challenges of a new technology and the health aspirations of a growing population.

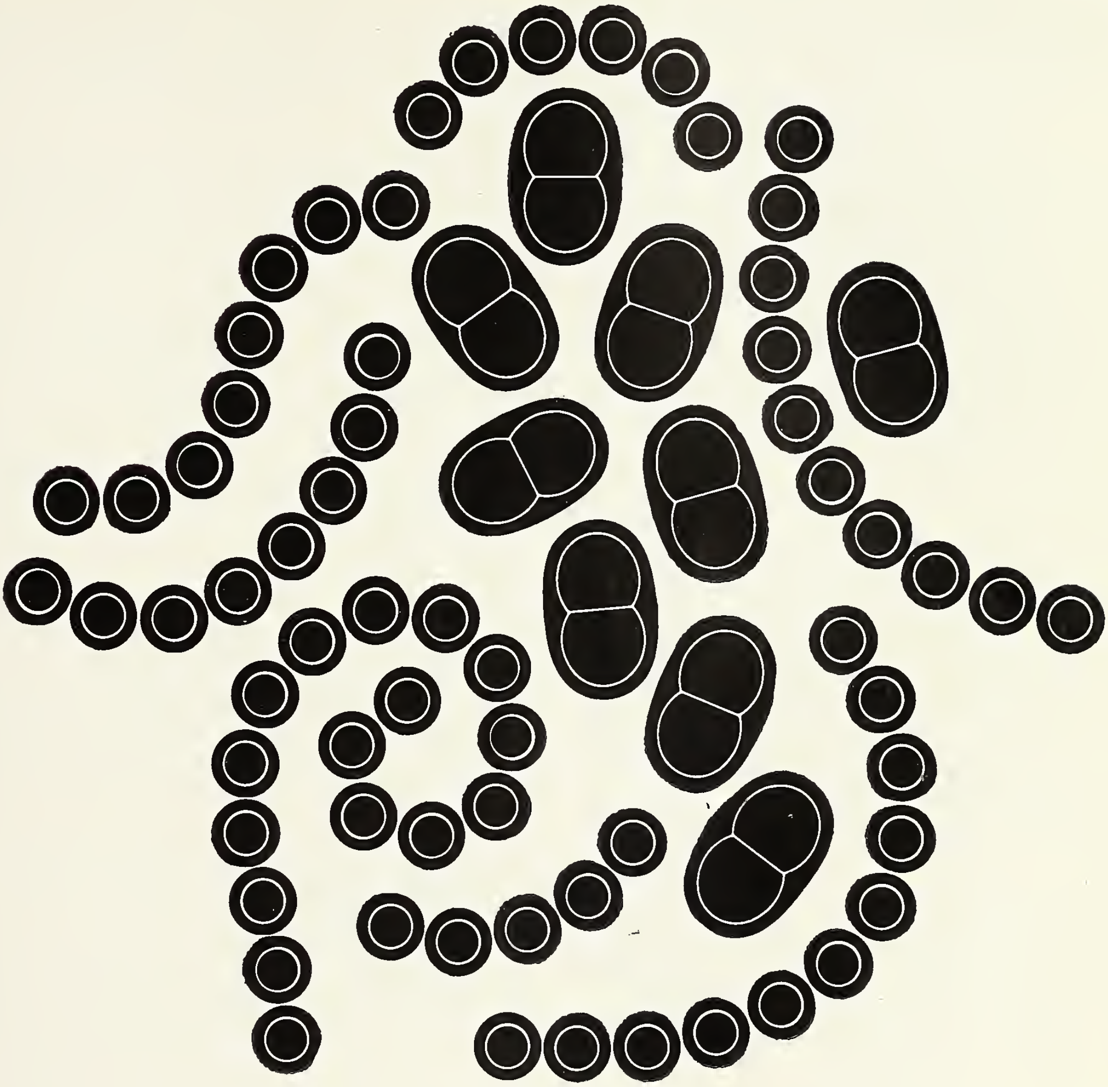
It should be made clear that P.L. 89-239 broke no new ground in advocating regionalization for medical planning. That had started long before the legislation was enacted; the Hill-Burton Act of 1946, for example, had been based on the concept of regionalization, and P.L. 89-239 represented simply an extension and fulfillment of that concept.

Physicians Represented

Finally, the regional medical program legislation requires that its objectives be accomplished "without interfering" with the patterns of medical practice and medical care. This has permitted the representatives of the medical profession, through membership on the 40-member advisory board, to declare when a program is consistent with the patterns of medical practice and medical care and when it is not.

P.L. 89-239 establishes no central authority for the development of individual programs. There is none here. Initiative for each activity stems from each participating agency or institution; direction of the activity likewise rests in local hands during its lifetime. CRMP assists to the extent of provid-

during and after infection



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ing staff help for the development of project requests, while its advisory board reviews all project proposals for their value in advancing the broader goals of CRMP before approval and maintains continuing audit to assure their sustained relevance.

It is interesting to note that there is no national model for regional medical programs. Though similarities obviously exist, each of the 55 programs in the United States is individually tailored to meet the health care requirements of its region. It follows, then, that application of the law differs from region to region. In some regions P.L. 89-239 is being applied on a narrowly conceived categorical basis, with projects quickly developed and funded in the form of mobile educational and testing units, nurse training programs, and similar showcase projects in heart disease, cancer, or stroke.

Broad Mandate

We in Connecticut, believing the mandate of P.L. 89-239 to be much broader, opted for an approach which would embrace the whole health care system. Far better for the people of Connecticut, it seemed to CRMP, to concern itself not only with improving our capabilities in the management of heart disease, cancer and stroke but with the total picture, so that victims of other diseases may be equally treated and—what is equally important—the preventive aspects of health appropriately emphasized.

The goal of CRMP is to make available the highest quality medical care to Connecticut's three million citizens in the most efficient manner. CRMP's task is to show how each segment of the health care system can help the other to achieve that goal.

SAVE-THE-DATE

Wednesday, June 10, 1970

22nd ANNUAL MEETING OF THE

CONNECTICUT HEART ASSOCIATION

HOLIDAY INN — Bridgeport, Connecticut

Title of Program

"SCREENING FOR CORONARY PRONENESS AND THE ROLE OF THE PRACTICING PHYSICIAN"

Keynote Speaker

WILLARD KREHL, M.D.

Professor and Chairman of the Dept.
of Preventive Medicine and Community Health
Jefferson Medical College — Philadelphia, Pa.

News From Yale University School Of Medicine

The University has been notified of the death of Dr. E. Richard Weinerman, Professor of Public Health and Medicine at the Yale School of Medicine.

Dr. Weinerman and his wife were passengers on the Swiss airliner which crashed near Zurich, killing everyone aboard. The plane was bound for Israel and news reports indicate that the crash was caused by sabotage by Arab terrorists.

Dr. Weinerman had left New Haven on a three-month sabbatical to study the health-care systems of Israel, Japan and New Zealand.

His findings were to be published in the form of a book, a companion volume to a recent study of health care systems of Eastern Europe, published by the Harvard University Press.

His previous studies over a period of more than a decade had taken him to Eastern Europe, Britain, France and the Scandinavian countries.

Dr. Weinerman was involved in the entire field of medical care and its organization and operation during the past 25 years, both in the United States and abroad and was particularly concerned with the quality of medical care.

He specialized in the development of methods for the study and observation of the quality of care and the training of health personnel for the improvement for medical care.

His experience covered almost all aspects of medicine, including service during World War II as the chief of a combat shock team in the European theater of operations, service with several government agencies, private practice in internal medicine, and involvement in administration and education.

A Hartford native, the 52-year-old physician was educated at Yale University and received his medical degree from Georgetown University. His specialty training was in internal medicine.

He returned to New Haven in 1962 from the West Coast where he was involved both in education and the practice of medicine, heading the department of ambulatory services at Yale-New Haven Hospital and teaching part-time.

He gave up this position in 1968 to become head of the section of health services administration at the department of public health and return solely to teaching and research.

Among his many publications in prominent medical and public health journals was a five-part research series, "Yale Studies in Ambulatory Services," a major study of emergency services.

He was a consultant to the Community Health Foundation, a member of the visiting committee of the Harvard University Health Services, consultant to the U.S. Public Health Service on Indian Health, a member of the Connecticut Advisory Committee to Medicaid and of the Committee of 100 for National Health Insurance at the time of his death.

He received the Senior Faculty award from the Commonwealth Fund in 1967, was chairman of the Medical Care Section of the American Public Health Association from 1965-68, was a past national president of Delta Omega, the public health honor society, and in 1950 was a traveling fellow for the World Health Organization (WHO).

Dr. Weinerman had stopped over in Geneva while on his way to Israel to discuss his research with WHO officials and make use of its international library.

Yale Medical School Dean Dr. F. C. Redlich said Dr. Weinerman was "admired at Yale and in New Haven by his colleagues, his students, and his patients. His questioning mind and his devotion to intelligent planning in the delivery of health care made him a pioneer and innovator on the national and international level as well."

Dr. I. S. Falk, professor emeritus of public health said "his loss at this time is an extremely great one, not only for Yale and New Haven—because of his extensive involvement in the developing programs at the Yale-New Haven Medical Center—but also for the whole field of medical care and public health in the United States."

AROUND THE STATE

NEW HAVEN COUNTY

New Haven County Medical Association 186th Annual Meeting

March 19, 1970

The 186th Annual Meeting of the New Haven County Medical Association was held at the Waverly Inn, Cheshire, on March 19, 1970. Kurt Pelz, of Wallingford, presided. There were 501 out of 1,042 members registered, which reflects upon the subleties of compulsory attendance currently in effect in Fairfield, Hartford and New Haven counties.

The Connecticut State Medical Society was represented by President Stevens J. Martin, President-elect Morris A. Granoff, Secretary Reginald C. Edson, Treasurer David A. Grendon, Speaker of the House Kenneth F. Brandon, Vice-Speaker of the House Frank K. Abbot and Executive Director William R. Richards.

The meeting was halted at the beginning for a moment of silent remembrance of the following members who passed away in 1969-1970: Eugene M. Blake 1882-1969, Abe S. Brown 1902-1969, Michael J. Conroy 1896-1969, Arthur Bliss Dayton 1889-1969, Theodore R. Dayton 1896-1970, Clyde L. Deming 1885-1969, George A. Leonard 1884-1969, Pasquale Lombardi 1890-1969, Maxom M. Senfield 1895-1970, E. Richard Weinerman 1917-1970.

The membership later elected the following new physicians to provisory membership in the New Haven County Medical Association: By Transfer from out of State Counties: Earl L. Baker, Derby; and Donald J. Weber, Waterbury. By initial direct application, William H. Baird, Wallingford; Andre R. Boissevain, Seymour; Remo Fabbri, Jr., New Haven; Chester S. Kucinski, New Haven; Jose D. Llibre, New Haven; Robert F. McGann, Meriden; David F. Musto, New Haven; Daniel S. P. Schubert, West Haven; Frank A. Sparrow, Wallingford; Marc J. Taylor, West Haven; and Joseph A. Vincitorio, Waterbury.

The annual elections resulted in the filling of the following posts: President, Stewart J. Petrie, Derby; Vice-President, James H. Root, Jr., Waterbury; Clerk, William L. West, Derby; Councilor Kurt Pelz, Wallingford (two years); Associate Councilor, Senior, James H. Root, Jr., Waterbury (two years); Associate Councilor, Junior, Jerome K. Freedman, New Haven (two years); Members Executive Committee, one year, Kurt Pelz, Wallingford. Member Credentials and Orientation Committee (three years), Howard Spiro, New Haven; Board of Censors (two years) Kurt Pelz, Wallingford; John Riesman, New Haven; William Arnold, Jr., Middlebury. State Legislation Committee (one year) Bernard A. Burnham, Waterbury, Chairman; (two years) Jerome K. Freedman, New Haven. Third Party Payments Committee (one year) Hubert Bradburn, New Haven; Joseph Fraknoi, Wallingford; Allan Goodyear, New Haven; Milton Jennes, Waterbury; Ely C. Wagshul, Meriden; George L. Wilson, New Haven, Chairman. Alternate Delegates to Conn. State Medical Society, one year (30 required) East Shore: Richard Rosenthal, Branford; William

VanEck, East Haven. Meriden: Arnold Franz, II, Meriden; Bernard Klein, South Meriden; Alfred St. James, Wallingford. Naugatuck Valley: Jack Holden, Derby; William Coyle, III, Derby. West Shore: Abraham E. Alpert, West Haven; Leonard Rapaport, Milford; Lawrence Tierney, West Haven. Waterbury: Bernard A. Burnham, Waterbury; Morris Coshak, Waterbury; John Elser, Naugatuck; Milton Jennes, Waterbury, Joseph Wihbey, Waterbury. New Haven: George A. Bonner, New Haven; Hubert Bradburn, New Haven; Mario G. Conte, New Haven; Pierino D'Elia, New Haven; Arthur Ebbert, Jr., New Haven; James B. Fanning, North Haven; H. Robert Greenhouse, New Haven; Florence Keller, Woodbridge; Saul Milles, Hamden; John Moench, New Haven; Walter S. Morgan, New Haven; Sherwin Nuland, New Haven; Dominic Schioppo, New Haven; Eugene Serafin, New Haven; William E. Swift, New Haven.

The usual donney-brook took place in the very necessary and democratic process of by-laws changes, some of which were passed, and others amended or defeated.

As usual, much of the time spent in the meeting revolved about these parliamentary matters. In addition, more of the same was guaranteed for next fall by the laying-on-the table of more such by-laws changes.

Three physicians presented ten minute resumes' of issues that are of considerable importance to the present-day medical scene. They were Dr. Bernard A. Burnham, of Waterbury; Dr. J. Alfred Fabro of Torrington; and Dr. William R. Richards of New Haven. Their presentations were well received and much appreciated, especially in view of the exceptional amount of time each doctor had to spend in managing to condense what he had to say into ten minutes.

During the course of the meeting it was frequently pointed out by many speakers and many members, that the pace of our activities seems to be closing in upon us. It often was said that there is an acceleration of events that tends to engulf us within a tide of fast-moving changes with which we are ill-equipped to cope. Each day there is more to do, with less time, on the part of less people, to devote to more tasks. There is a rapid increase in the number of problems, the number of decisions, the number of proposed programs, the number of thrusts to which we are asked to direct ourselves at a time in which we find ourselves ill-equipped for the task.

Visible evidence of these fast-moving matters that were voiced at the meeting included remarks about:

1. The doubling of malpractice insurance rates in the past year and a half in Connecticut, and an even greater increase in California.
2. The Himler-Budd Report on AMA Reorganization.
3. The Hartford Foundation Project submitted to the Conn. State Medical Society.
4. The Conn. State Medical Society Council's Reorganization Plans.
5. The Interstate Reciprocity of physician licensing proposal.
6. The AFL-CIO National Compulsory Health Insurance Report.
7. The AMA National Health Insurance Proposal.
8. The Senate Finance Committee Hearing on Drug Abuse and that committee's recommendations.
9. The Senate Finance Committee hearings on Medicare and Medicaid with that committee's recommendations.
10. The Regional Medical Planning Project and most specifically CRMP in Conn.
11. The Partnership in Health Project, especially in Connecticut.
12. The Regional Hospital Planning Project.
13. The CDAP Project both in New Haven and State-wide.
14. The Regional Community Health Planning Councils.
15. The Proposed merger in H.E.W. of various "planning agencies" into one large super "planning agency".
16. The effect of COMPAC, the Conn. State Legislature, Congress, and H.E.W. on the future ways of "delivery of medical care" and how its effect will affect current concepts of medical care.
17. The problems of media attitudes towards organized medicine including newspaper "editorial" bias.
18. The problems of "consumer" attitudes towards "the health care industry".

The New Haven County Medical Association has begun a pilot program in Public Relations by contracting for the services of a paid professional public relations firm, The Lee Isenberg Associates of Hartford. A pilot project will be developed to improve both the internal and the external communications of the Association.

Following the business meeting, an over-flow crowd of 367 enjoyed a roast beef dinner and participated enthusiastically in the door prize drawings

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At the dinner, Mrs. Peter Fiskio, President of the New Haven County Medical Association Woman's Auxiliary, reported on the activities of her organization. Mrs. Fiskio's report of a record-breaking realization of over $2,000 for the Scholarship Fund from the Burgundy Ball received an enthusiastic commendation from the assembly. President Fiskio urged the male physicians of the county to let their wives know that the Auxiliary is seeking new members to augment their present small but active and dedicated membership.

Dr. Stewart J. Petrie, incoming President, presented Dr. Kurt Pelz, outgoing President, with the traditional Past President's Plaque. In the presentation, Doctor Petrie complimented Doctor Pelz as being a man of tact, dedication, understanding, and most of all . . . a gentleman. He expressed his regrets that the Association could not have had the benefits of Doctor Pelz' leadership for more than just the short year passed.

In responding, Dr. Pelz expressed his gratitude for the cooperation he had received from the membership during the year; urged that the Association consider a longer term of office for the President in order that a President can follow through his programs; and concluded with the same remark of confidence in the membership that was quoted in the New Haven Register a year earlier when he took office, by saying "I (still) think you're a nice bunch of fellows".

Respectfully submitted,
William L. West, M.D., Clerk

MEETINGS

Conference on Changing Role in Nurse-Physician Relationship in the Delivery of Health Care Service

Park Plaza Hotel, New Haven, Connecticut

Wednesday, May 27, 1970 9:45 A.M.-4:00 P.M.

Registration Fee $5.00 (includes luncheon)

Advance registration necessary and may be made with the Connecticut State Medical Society office, 160 St. Ronan Street, New Haven.

Doctor's Office

Julio E. DeMarchena, M.D. announces the opening of his office for the practice of orthopaedic surgery, 67 Central Avenue, Waterbury, Connecticut 06702.

Daniel A. Hart, M.D. announces the opening of his office for the practice of Internal Medicine at Bradley Memorial Hospital, Southington, Connecticut.

Albert J. Levis, M.D. announces the opening of his office for the practice of psychiatry, 299 Washington Avenue, Hamden, Connecticut 06518.

Harry B. Soletsky, M.D. announces the opening of his office for the practice of cardiology and internal medicine, Route 7, Brookfield, Connecticut 06804.

Vera M. Stallworth, M.D. announces the opening of her office for the practice of surgery in the Washington Medical Building, 1026 Park Avenue, Bridgeport, Connecticut.

Zuli Steremberg, M.D. announces the opening of an office for the practice of internal medicine and cardiology at 2660 Main Street, Bridgeport, Connecticut.

William D. Troy, M.D. announces the removal of his office from 116 Summer Street to 140 Hoyt Street, Stamford, Connecticut.

The Connecticut State Medical Society offers placement assistance through the Physicians Placement Service, 160 St. Ronan Street, New Haven, Connecticut, 06511. This service is for the use of physicians seeking locations, as well as physicians seeking associates, and is without charge.

Letter To The Editor

Members of the Society are invited to communicate with the Editor expressing their opinions or giving information as to any matter of interest to the members. The Editorial Board reserves to itself the right to select the communications or excerpts therefrom that will be published and to reject others. As with other material which is submitted for publication, all letters will be subject to the usual editing. Address all correspondence to: THE EDITOR, CONNECTICUT MEDICINE, 160 St. Ronan Street, New Haven, Connecticut 06511.

To The Editor:

The first steps in self-improvement should logically be self-awareness and self-criticism, followed by the seeking of solutions to the problems thereby disclosed. In such a process, American medicine is reaching the point at which knowledge of the methods by which other medical communities have solved their health delivery puzzles can feed our hunger for answers to our own. Accordingly, Connecticut physicians need to know about the origins, objectives, achievements and shortcomings of such solutions as the English have found in their National Health Service. For this reason, it is clear that *Connecticut Medicine* is filling a real need in planning a series of articles as begun in the January issue.

However, it is exactly because of our need to have such information that I write to take issue with the prejudgement implicit in the first communication by Ned Thomas. This article, in my view, presents a perspective of the Health Service which could lead to considerable misconception on the part of readers who have no previous knowledge of the scheme. In the first place, Mr. Thomas states that the Service has "no compulsion about it" because everyone is free to use or not use its facilities. The fact that the scheme continues in existence is then used by him as an "obvious commentary on how they feel about it."

The facts in the initial statement are true as far as the voluntary aspect of utilization are concerned, but it should be made clear that payment is compulsory whether services are used or not. In a society in which a consumer is forced to pay for a service, the fact that he then utilizes that service, when needed, rather than duplicating his payment to get it elsewhere, is hardly as obvious a commendation as Mr. Thomas would have us believe.

In fact, it would have been germaine to this aspect of a really unbiased report to let the readers of this *Journal* know that private health insurance schemes are now a very big business in the United Kingdom, with large numbers of those who have the means seeking private care for major illnesses, while utilizing the Health Service for minor problems, eyeglasses and prescriptions. Most English consultants have a long list of private patients. Their willingness to pay twice in order to avoid Health Service care may be a much more significant and "obvious commentary on how they feel about it."

Mr. Thomas is a science writer of considerable repute in Connecticut. I find it staggering that he should consider unweighted statistics on comparative tuberculosis and poliomyelitis mortality between 1950 and 1967 as any sort of index of how well a scheme of health care delivery has worked. Mr. Thomas should, for his readers' information, compare these statistics with those of other countries in which the health delivery system has not changed markedly in the intervening years, such as the United States or Russia. Such comparisons would tell us something about the role of the system in improving the statistics.

During a brief professional contact with the National Health Service in 1959, I found much to admire and much to criticize. In our need to improve the climate and operation of our own system we must have clear evidence, and not prejudged opinions, partial expositions and unscientific comparisons. I look forward to finding such evidence in Mr. Thomas' later articles.

Very truly yours,

Sherwin B. Nuland, M.D.
2 Church Street South
New Haven, Conn. 06519

Communications such as this are welcome. Mr. Ned Thomas is now in Israel. When he returns, such letters will be submitted to him for comment. —Editor

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June, 1970, will mark the 20th anniversary of the Connecticut Red Cross Blood Program. From a faltering start, this newest of Red Cross programs probably touches more lives with its potential for good than almost any other.

Yankee tenacity may be the reason why, in the face of many difficulties, three New England states have continued to support so-called "total" blood programs. Stubbornly and courageously resisting easier methods, Connecticut, New Hampshire and Vermont are the triumvirate in the country furnishing blood without cost to all hospitals within their borders.

The system, depending upon thousands of volunteers, is conducted by the Red Cross. In Connecticut, 37 Red Cross chapters handle the tremendous task of finding suitable sites for bloodmobile drives, recruiting donors, collecting, processing, storing and distributing blood and its by-products. In addition, the agency keeps up a running program to inform the public on the needs and uses of blood.

As a result, if you need a transfusion while you're a patient in a hospital anywhere in the state, the Red Cross will see that you get the blood. All the blood you need, when you need it. And without charge.

Hospitals necessarily charge for administering blood, but the fluid itself, or its components, are free.

In the last fiscal year, the Connecticut Red Cross Blood Program distributed 114,561 units of blood to the state's 45 hospitals, for the use of patients. Every drop was contributed by a voluntary donor at a blood bank or at a hospital in response to a Red Cross call.

Under the "total" program as conducted here, non-residents hospitalized while in the state have similar claims to blood. Not only is it furnished without charge, but there is no pressure on recipients or their families to replace the quantity used.

Throughout the country the system most commonly followed makes blood available on an insurance or replacement basis. This usually works out as pint-for-pint or double the quantity transfused. If not replaced, the patient must pay upwards from $25. per pint. Costs soar when demand out-paces supply.

Collections made at bloodmobile drives daily throughout the state are delivered to the Blood Center, 100 Farmington Avenue, Hartford, for processing and distribution. To meet ordinary day-to-day requirements, the Center is geared to collect 2,250 units per week. If donations slump, the Red Cross rounds up donors to give at hospital blood banks.

Helping to speed the job is a traveling laboratory that processes donations within minutes. First of its kind in the nation, it has been visiting Connecticut communities since early March. A crew of technicians operates the fully equipped laboratory, which checks samples for more than 20 blood factors. Rare combinations are listed with the national file on blood donors at the agency's headquarters in Washington, D.C.

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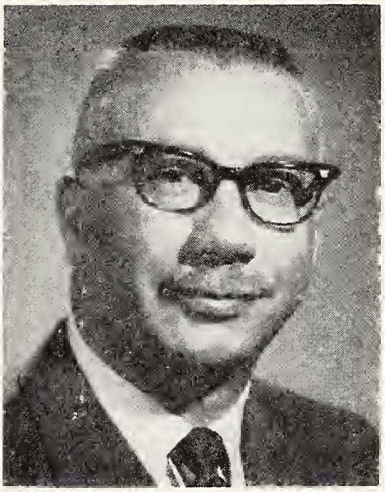
New York City, New York
JUNE 21-25

OBITUARY

Samuel Jaffe, M.D.
1913-1970

Death from a massive myocardial infarction suddenly and unexpectedly claimed the life of Dr. Samuel Jaffe while he was on vacation in Miami Beach, Florida, on March 29, 1970.



Born in Colchester, Connecticut, he was graduated from Bacon Academy. After he received his bachelor's degree from the University of Connecticut, he earned his medical degree from the Bellevue Medical School of New York University in 1938.

Upon completing an internship and surgical residency at the old Grace Hospital in New Haven, he served during World War II in the U.S. Navy, achieving the rank of Commander. On returning to civilian life, in 1946, he opened his office for the private practice of surgery. He served on the surgical staffs of Yale-New Haven Hospital and the Hospital of St. Raphael in New Haven.

Professionally, Dr. Jaffe was exceptionally devoted to his patients, and enjoyed a busy practice. He became a Diplomate of the American Board of Surgery, a Fellow of the International College of Surgeons, and a member of the American Board of Abdominal Surgeons. In addition, he was a member of the New Haven Medical Association, New Haven County Medical Association, the Connecticut State Medical Society, and the American Medical Association.

His concern with civic affairs was evidenced by his serving as President of the Jewish Home for the Aged in New Haven for many years.

Those who knew Dr. Jaffe personally were heartened by his warm, reassuring manner (his devotion to his family and friends, and his sportsmanship.

His death not only leaves a void in the hearts of his family and friends, but also represents a sad loss to the community to which he gave so much.

I quote from Richard LeGalliene:

> ". . . How many friends I loved are gone!
> Death delicately takes the best . . ."

Samuel Spinner, M.D.

In Memoriam

Clark, William T., Bridgeport, Queen University (Kingston, Ontario) 1934. Dr. Clark was a surgeon in the Bridgeport area more than 25 years and physician for the Bridgeport Brass company. He was a consulting physician at Bridgeport Hospital. Dr. Clark served in the United States Army during World War II. Dr. Clark was a member of the American Medical Association, Fairfield County Medical Association, and the Connecticut State Medical Society. Dr. Clark died March 22 at the age of 64.

Dayton, Theodore R., Redding, Harvard Medical School 1925. Dr. Dayton specialized in pulmonary diseases. He was appointed surgical officer for the Peter Bent Brigham Hospital, Boston, under Dr. Harvey Cushing, and was subsequently appointed Cushing Fellow at Yale Medical School. Dr. Dayton served as chief surgeon at Laurel Heights State Sanitarium in Shelton and was on the staff of Gaylord Farms Sanitarium, Wallingford. He was manager of the U.S. Veterans facility in Rutland Heights, Mass., and in Baltimore, until his retirement in 1956, after which he served on the staff of the Veterans' Administration Hospital, West Haven. Dr. Dayton was a fighter pilot in World War I. Dr. Dayton was a member of the American Trudeau Society, American College of Chest Physicians, American Medical Association, New Haven County Medical Association and the Connecticut State Medical Society. Dr. Dayton died March 15 at the age of 74.

Little, Milton F., Hartford, Yale University 1928. Dr. Little was an ophthalmologist in the Hartford area since 1933. He was on the staff of the Hartford Hospital and the McCook Hospital. Dr. Little was a member of the American Medical Association, Hartford County Medical Association, Connecticut

State Medical Society and the New England Ophthalmological Society. Dr. Little died March 29 at the age of 68.

Metcalf, Elliott H., Rockville, Jefferson 1914. Dr. Metcalf was a general practitioner and surgeon for over 50 years in the Rockville area. He was a pharmacist in Rockville before becoming a physician. During World War I he served as a physician and surgeon with the American Ambulance Corps in France and was in charge of the Corps ward in Neuilly. Alter completing his service he returned to Rockville and started his practice in 1920. In December 1969, the highest honor ever to be given a Rockville resident was bestowed upon Dr. Metcalf when Mayor McCoy in the first official proclamation of its kind in the history of the town, named "Dr. Metcalf Appreciation Day." Also a similar resolution was passed by the board of trustees of Rockville General Hospital. Dr. Metcalf was Vice-President of the Rockville City Hospital. Dr. Metcalf was a member of the American Medical Association, Tolland County Medical Association and the Connecticut State Medical Society. Dr. Metcalf died February 24 at the age of 81.

Segal, Jacob, Manchester, Tufts 1928. Dr. Segal was an internist in the Manchester area for the past 30 years. He was chief of cardiology at the Manchester Memorial Hospital since 1955. He was a member of the American Medical Association, Hartford County Medical Association and the Connecticut State Medical Society. Dr. Segal died April 7 at the age of 67.

Simonton, Frank F., Enfield, Bowdoin Medical School of Medicine 1903. Dr. Simonton was a general practitioner in the Enfield area since 1911. He served as town health officer for 16 years from 1926 to 1942; and as medical examiner in Enfield for 20 years from 1926 to 1946. Prior to his coming to Enfield, he practiced medicine and surgery in Ellsworth, Maine for eight years. While a resident of that town, he served as mayor in 1908. Dr. Simonton was commissioned a captain in the medical corps during World War I in 1918, he also served as a former member of the local draft board during World War I. Dr. Simonton was a member of the American Medical Association for more than 67 years, Hartford County Medical Association and the Connecticut State Medical Society. Dr. Simonton died March 4 at the age of 93.

Weinerman, Edwin R., New Haven, Georgetown 1942. Dr. Weinerman specialized in Internal Medicine. A professor of public health and medicine at the Department of Epidemiology and Public Health at the Yale School of Medicine. Dr. Weinerman left New Haven on a three-month sabbatical to study the health-care systems of Isreal, Japan and New Zealand. His findings were to be published in the form of a book, a companion volume to a recent study of health care systems of Eastern Europe, published by the Harvard University Press. He headed the department of ambulatory services at Yale-New Haven Hospital and was teaching part-time. He gave up this position in 1968 to become head of the section of health services administration at the department of public health and returned solely to teaching and research. Dr. Weinerman was a consultant to the Community Health Foundation and on the staff of the Yale-New Haven Hospital. Dr. Weinerman was a member of the American Medical Association, New Haven County Medical Association, and the Connecticut State Medical Society. Dr. Weinerman died February 21 at the age of 52.

Yeager, Charles F., New Jersey, Hahnemann 1933. Dr. Yeager formerly lived in the Easton area of Connecticut. He served at Remington Arms for nearly 34 years as a medical director before his retirement in 1968. He was considered among the foremost practitioners of occupational medicine, moving into the field after having been engaged in private practice. Dr. Yeager was appointed medical supervisor of all Remington Plants, in 1942 and, in 1943, became chief medical supervisor of the Company. In 1952, he was named medical director. In 1955, while he was chief medical consultant to the State Bureau of Vocational Rehabilitation, Department of Education. Dr. Yeager had been a member of the consulting staff of Bridgeport hospital and the courtesy staff of St. Vincent's hospital. He served as secretary-treasurer of the Industrial Medical Association of Connecticut; as chairman of the Connecticut State Medical Society's Committee on Industrial Health, and the first vice-president of the Society in 1946. In 1949, he was elected president of the New England Conference of Industrial Physceians and Surgeons. Dr. Yeager was a member of the American Medical Association, the Bridgeport Medical Society, the Fairfield County Medical Association and the Connecticut State Medical Society. He died February 26, 1970 at the age of 66.

Unexplained Dizziness May Be Due To Transient Arrhythmia

(*JAMA*, 210: 1842, December 8, 1969) When there is no apparent reason for a patient's dizziness or fainting, the physician should consider the possibility of transient cardiac arrhythmia.

Dizziness and fainting can indicate cerebral ischemia. Transient arrhythmias may not lead to cerebral ischemia in normal persons, but can lead to either diffuse or focal cerebrovascular insufficiency in patients with cerebral artery narrowing, an investigator from the Emory University School of Medicine, Atlanta, reported to the American Heart Association meeting in Dallas.

Paul F. Walter, M.D., fellow in cardiology at Emory, said continuous ECG monitoring of 39 patients revealed ten transient arrhythmias or conduction abnormalities "which probably precipated their neurologic symptoms."

In seven cases, the patient's symptoms were what might be expected to result from the arrhythmia. In the other three, the cause of the neurologic symptoms remained unclear because of the patient's senility or other illness.

"Appropriate treatment of the heart rhythm disturbance abolished the symptoms of dizziness or fainting in most of these patients," the investigator reported.—L.H.N.

Observations On The Culture Diagnosis Of Gonorrhea In Women

(*JAMA*, 210: 312, October 13, 1969, Schmale, John D., Martin, John E., Jr. and Domescik, Gerald) In the past six years, the number of reported cases of gonorrhea in the United States has increased from 270,000 in 1963 to 431,000 in 1968. Since the majority of cases go unreported, the true incidence at present is estimated to be closed to 1,500,000.

Because of this continued increase in the number of gonococcal infections, there is a necessity for rapid and accurate diagnosis of the disease. A gram-stained smear of the urethral exudate remains the optimal diagnostic method in the male, but because of the large number of various bacteria naturally occurring in the female urogenital tract, a gram-stain diagnosis is unreliable in women. For this reason, culture diagnosis has been advocated in females. Before 1966, diagnosis by culture was time-consuming and tedious at best, and it was often impossible because of overgrowth of the plate with naturally occurring flora. But, with the advent of the Thayer-Martin selective culture medium, rapid positive culture diagnosis became possible for gonorrhea. This medium contains inhibitory antibiotics (vancomycin hydrochloride, colistimethate sodium, and nystatin) which allow growth of pathogenic *Neisseria* while almost completely suppressing the growth of contaminants.

A study to determine which site or sites should be cultured in the female to detect the greatest number of infected patients has not been performed with the Thayer-Martin medium. Lucas et al cultured specimens from three sites (cervix, vagina, and urethra) on Thayer-Martin medium but did not include the rectal site in the study. This present communication reports the results of a study employing the Thayer-Martin medium on which specimens from the cervix, urethra, vagina, and rectum were cultured. Of the four sites examined, the cervix was the single site with the greatest frequency of positive cultures. However, we suggest that at least two culture sites be utilized; our results show that the cervical and rectal sites gave the greatest frequency of detection when specimens from two sites were cultured.—L.N.H.

Perinatal Care In Diabetics

(*JAMA*, 210: 801, November 3, 1969) The value of urine estriol measurements in the management of pregnant diabetic women has been shown in a study conducted at the University of Southern California, reports Gail V. Anderson, M.D.

According to Dr. Anderson, professor of obstetrics and gynecology at the School of Medicine, perinatal mortality in diabetic women can be reduced by as much as 50% with the help of serial estimates of urine estriol.

Nine of the 16 perinatal deaths in a series of 186 patients with varying degrees of carbohydrate intolerance might have been avoided, he said, if the assay results had been applied. To determine the value of the assay, estriol levels were determined, but the results were not used to influence clinical management of these patients.

The "estriol preventable deaths" included babies dying of respiratory distress syndrome and/or other complications of prematurity. Estriol levels were satisfactory in these women, he said, and the early elective delivery might have been safely postponed. In some patients, delivery was postponed in spite of the fact that estriol levels were low or falling rapidly. The outcome was a stillbirth.

Estriol levels under 4 mg per 24-hour urine collection after 34 weeks gestation, or a rapid decline of over 60%, were thought to be signs of actual or impending death of the fetus. Estriol values were considered valid only if estimations of creatinine were between 800 and 1800 mg per 24-hour urine specimen.

In 31 normal control patients, weekly estriol determinations, from 29 weeks until delivery, showed no value in the danger zone. There were no perinatal deaths.

Of the 186 patients in the test series, 49 were taking insulin or oral hypoglycemic agents. Two perinatal deaths occurred in the 10 patients with the most severe form of diabetes (Class D).

There was also one estriol preventable death in the 7 patients with Class C diabetes, and one in the 32 patients with Class B. In the 137 Class A patients who were not dependent on insulin but showed varying degrees of carbohydrate intolerance, there were 8 perinatal deaths. Dr. Anderson said 5 of these 8 deaths, all associated with early delivery, might have been prevented if estriol values had been used in management of the patient.—L.H.N.

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Diabetes Masks Vitamin Lack

(*JAMA*, 210: 445, October 20, 1969) Dr. Wakefield and associates found that 88 of 402 diabetics studied had unequivocal evidence of neuropathy. Of these, eight (about 9%) showed malabsorption and low serum levels of vitamin B12.

All diabetic patients are now being screened for the vitamin B12 deficiency. Of the original eight patients, one died of unrelated condition; one with optic atrophy is not improved; and a third, age 75, was seriously disabled before commencement of B12 therapy.

The study emphasizes the importance of considering vitamin B12 deficiency in cases of diabetic neuropathy. Since about 20% of the patients in the study had neuropathy, "when one considers the total number of diabetics at risk that is a lot of people. They found 10% of patients with diabetic neuropathy to have vitamin B12 deficiency, but even a much smaller percentage would indicate that the dual pathology is not uncommon."—L.H.N.

Federal Cuts To Universities Continue To Dwindle

(*Scientific Research*, 4 No. 25, 19 December 8, 1969, Lipkowski, W., Washington Science Outlook) Senator Warren Magnusen of Washington has said he hoped to do something about cuts directed by the Budget Bureau that would reduce the number of graduate level students in all health professions by about 11,000.

Contrary to the popular belief in Congress U.S. Universities are finding it hard to keep their heads above water as federal budgets for science and higher education continue to dwindle. That is the message of a nearly completed National Science Foundation survey on the effects of the budget cuts on the nations colleges and universities. These institutions had "had to dig into their own resources" says one top NSF official.

Among the hardest hit are the newer emerging institutions which have yet to build their reputations. They have an urgent and immediate need for funds to pay for top-flight faculty and building construction.

The NSF survey also uncovered an ominous side effect of the cutbacks: the tendency of scientists to limit their proposals to "safe" research—research sure to bring practical results.—L.H.N.

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Index to Advertisers

Arch Laboratories, St. Louis, Mo. — — — — — — — 382
Bio-Chemical Procedures — — — — — — — — — — — 299
Burroughs-Wellcome, Tuckahoe, N.Y. — — — — 304 & 305
Campbell Soup Company, Camden, N.J. — — bet 336 & 337
Classified — — — — — — — — — — — — — — — — 361
Conal Pharmaceuticals, Chicago, Illinois — — — — — IBC
Dentocain Co., Bloomfield, Conn. — — — — — — — — 311
Dow Chemical Co., Midland, Mich. — — — — bet 304 & 305
Arthur W. Eade, Hamden, Conn. — — — — — — — — 375
Geigy Pharmaceuticals, Ardsley, N.Y. — — — bet 304 & 305
Geriatric Pharmaceutical Corp., Floral Park, N.Y. — 313, 319
Hall-Brooke Hospital, Westport, Conn. — — — — — — 304
Hynson, Westcott & Dunning, Inc., Baltimore, Md. — — — 3
Lederle Laboratories, Pearl River, N.Y. — — — 5, 364, IBC
National Drug Co., Philadelphia, Pa. — — 2, bet 244 & 245
Eli Lilly & Co., Indianapolis, Ind. — — — — — — — FC, 10
McNeil Laboratories, Inc., Fort Washington, Pa. — — — 301
Merck, Sharp & Dohme, West Point, Pa. — — 308, 309, 310
National Drug Co., Philadelphia, Pa. — — 2, bet 368 & 369
Poythress, Wm. P., Richmond, Va. — — bet 304 & 305, 305, bet 336 & 337
Roche Laboratories, Nutley, N.J. — — — — — — 6, 371, BC
Sanibel Hospital, Inc., Middletown, Conn. — — — — — 315
Searle & Co., G. D., Chicago, Ill. — — — — — bet 336 & 337
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Action of psychotropic drugs on the brain.
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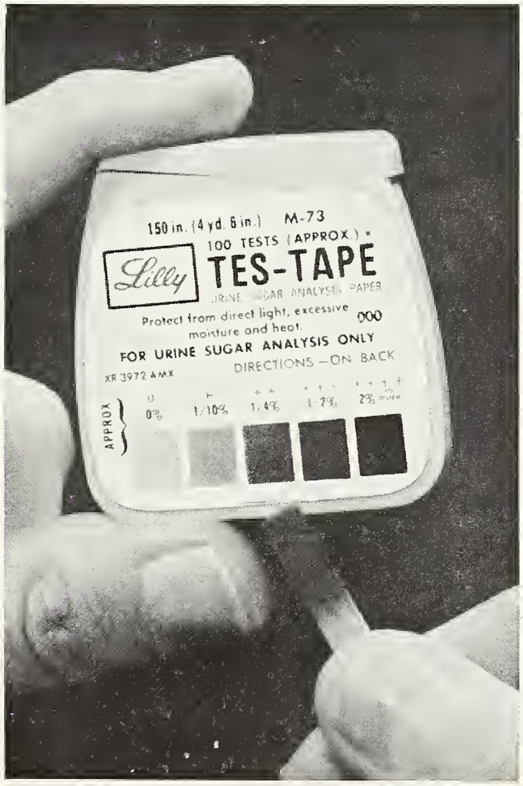

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CONTENTS

editorials

Drugs, Dreams And The Coronary Patient 385
The Courts Will Help To Resolve The Environmental Crisis 386
Medical Science And Practice In The Next Decade 390
An Institution For Environmental Studies: Redesigning The Environment 391
When To Use A Transvenous Catheter Pacemaker 393
Some Complexities Of Small Intestinal Physiology 394
Exercise Training For The Patient With Chronic Obstructive Pulmonary Disease 395
L-Dopa In Parkinsonism 396
Viruses And Cancer: Herpes Virus Vaccine Protects Against Marek's Disease Of Chickens 398
The Financial Pinch On Science 399

scientific

Pharmacodynamics Of 3, 4-Dihydroxyphenylalanine (Dopa) In Parkinson's Disease, *Melvin H. Van Woert, M.D.* . . . 401
Vaginal Antibiotic For Surgery, *Burton H. Cohen, M.D.* and *Philip DiSaia, M.D.* 406
Sacrococcygeal Teratoma Of The Fetus Complicating Pregnancy, *Vincent Pepe, M.D., Kynm S. Pynn*, and *Rolf E. Katzenstein, M.D.* 411
Post-Myocardial-Infarction Syndrome With Anemia, *Morton Glasser, M.D.* 413

departments

The President's Page 415
From The Executive Director's Office 417
Physician's Placement Service 421
Woman's Auxiliary 449

miscellaneous

Summary Of Proceedings Of The House Of Delegates . . . 426
  Address Of The President 429
  Report Of The Secretary 431
Around The State 433
X-Ray Of The Month, *Arnold B. Rilance, M.D.* 434
Electrocardiogram Of The Month, *Hyman N. Chernoff, M.D.* 436
Law-Medicine Notes, *J. Alfred Fabro, M.D.* 439
Letter-To-The Editor, *Hyman A. Levin, M.D.* 442
British National Health Services, *Ned Thomas* 444
The Connecticut Regional Medical Program, *Henry T. Clark, Jr. M.D.* 446
Obituaries:
  Charles Christopher Wilson, M.D. 447
  Jacob A. Segal, M.D. 447
In Memoriam 448
Laboratory Notes 452
Science News 453
New Books In Review 458

Connecticut Medicine

editorials

Drugs, Dreams And The Coronary Patient

We dream in a series of cycles each night. These cycles seem to be necessary to us. If they are forcibly suppressed the subject is unhappy and when he is left to make up for lost dreaming time, he promptly dreams to excess. Normally the total dreaming time amounts to about 100 minutes a night divided into several periods intercalated in cycles of about 80-110 minutes. The length of the cycle is inversely related to the metabolic rate of the animal, being longest in the elephant and very short in the mouse (5-10 min.).[1]

During sleep in man the brain and peripheral system under its control show continuous oscillations with a periodocity of about 90-110 minutes. At one extreme of the period the arousal is difficult, heart is slow and steady and the mental content if anything is thoughtful. At the other extreme of the cycle is the dreaming phase in which sleepers report hallucinoid dreaming.

Many things happen during the dreaming part of sleep. For example there is an anti-diuretic effect associated with release of antidiuretic hormone and water retention by the kidney. There also occurs during sleep a cyclical release of ACTH, glucocorticoids, and catecholamines.[2] This is the reason why about 20 per cent of patients with coronary attacks occurred while the patients were asleep. According to Nowlin 4 of his patients experienced 39 episodes of nocturnal angina pectoris probably during dreaming, when catecholamines are released and the myocardium requires more oxygen and develops hypoxia in the presence of coronary artery insufficiency. The released glucocorticoids cause loss of potassium and magnesium and increase in sodium and this sets up a vicious circle and aggravates the hypoxia.[3]

Equally the imbalance disturbs cardiac conduction and contractility with consequent likelihood of arrhythmias. Thus sleep entails periodic danger for coronary patients from potentially serious arrhythmias and myocardial ischemia sufficient to cause death in the absence of fresh coronary occulusion.[4] It is, therefore, important to know how REM sleep can be affected by drugs and other means so as to reduce the hallucinatory nature of dreaming. A number of workers have reviewed effects of drugs on dreaming at a Symposium of Carl Newberg Society recently published.[5]

THE COVER

Figure 1 summarizes the data available on four classes of drugs in the treatment of mental disorders. A study of this table will reveal some fundamental differences among these drugs which, when correlated with the symptomatology of various disorders, give some insight into the proper use of drugs in specific disorders. For example, symptoms of depression can be divided into (1) mood disturbance with a pervasive affect of depression, (2) biological disturbances including those of sleep, appetite, sex and automatic functions, and (3) psychological disturbances. If we look at the drug action of barbiturates, meprobamate, phenothiazines, and tricyclic antidepressants, we can discern that if we are going to pick *a priori* the right drug for the treatment of depression, it would be the tricyclic compounds. The data speaks for itself: (1) This drug stimulates the limbic system and therefore improves mood. (2) It stimulates the hypothalamus and therefore improves the various biological dysfunctions present in depression such as decreased appetite, sleep, and libido. (3) It inhibits the reticular formation, which further improves the sleep disturbance. (4) It increases the neurohumoral depots, which are thought to be deficient in depressive disorders. None of the other drugs have these combined properties.—William W. K. Zung, M.D., Assistant Professor, Duke University Medical Center and Veterans Administration Hospital, Durham, N.C.

The physiological concomitants of dreaming have received more attention than the content of dreams mainly because of the difficulty of quantifying or analyzing dream content statistically. However, Hall and Vande Castle[6] showed that the greater the ego strength of the dreamer, the less bizarre, elaborate and emotional are his dreams. In other words a person who is functioning well psychologically is not going to have intense or interesting dreams. Dream content is affected by experiences before sleep. There is a counter-balance here for the person given a relaxant before sleep will have dreams of activity while the person who has exercised vigorously will have a more peaceful dream. If he has been solving problems his dream will likely be a simple one. It would seem then that coronary patients who exercise daily within their capacity or spend time evenings in problem solving will tend to have more peaceful dreams.

One of the obvious questions is whether drugs given to relieve mental symptoms will change sleep patterns. Barbiturates are known to make dreams more thoughtful, but also reduce dreaming time by a small amount. Meprobamate and amphetamine have also been shown to cut down REM time.[7] Oswald of Edinburgh has also shown that a tranquilizer can abolish REM sleep, but withdrawal of the drug leads to excessive REM sleep and also almost nightmares.

Hartmann of Boston has studied a number of drugs and has confirmed the effects of barbiturates on slight reduction of dreaming time and making dreams more thoughtful and less hallucinatory. All antidepressants reduce REM time markedly, amitriptyline reduced it from 100 to 38 minutes a night and so does alcohol. Very few drugs increase REM time, these include reserpine, LSD and 1-tryptophane. Subjects with a full ration of REM time enjoy a good night's sleep. This makes one wonder whether drugs that cut down REM time may not be damaging to the individual. However, according to Hartmann some of these drugs simply reduce the need for REM, for there is no rebound after withdrawal. Antidepressants are in this category. It seems that by reducing the need for REM sleep time, antidepressants break a vicious circle of poor sleep—need for dreaming time—worse depression (see front cover).[7]

Since dreams may be considered the "psychoses of the night", it is of interest to see how dreams are affected by tranquilizers which are so effective against psychotic symptoms. In the Newberg Symposium Ornstein et al of Cincinnati contributed a study of dreams in schizophrenics treated with tranquilizers and showed that in patients being treated with the major tranquilizers, dreams tended to be more vivid but less frightening and less recall. The same group also discussed drug effects from the standpoint that intoxication and dreaming have much in common.

Freud in his "Civilization and its Descendants" pointed out man's need for palliatives to withstand the world's miseries and frustrations, one of the palliatives being an intoxicant. Both intoxicants and dreams bring us pleasure and temporary independence from the outer world. The coronary patient whose ego is strong and who exercises and indulges in some creative activity, especially in the evening, is less likely to need intoxicants or barbiturates to convert his dreams from hallucinatory to more thoughtful content.

We should not overlook the fact that every drug is a psychopharmacologic agent also because of its placebo effect which is manifested by the appearance in the dream of what the drug means to the patient, this being separated from any specific effect which the drug may have.

L.H.N.

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The Courts Will Help To Resolve The Environmental Crisis

Environmental problems usually represent conflicts between competing uses of natural resources. For example a virgin forest may be preserved as a wilderness or reduced to pulpwood. A city park may be kept for recreation or given over

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as a right of way for a freeway. It is natural, therefore, that lawyers with expertize at resolving conflicts should be called upon to help resolve problems concerned with the environment. We find numerous legal actions over environmental issues are now pending before various courts and administrative agencies around the country. They include suits and petitions to outlaw use of DDT, to prevent completion of a Corps of Engineers Cross Florida barge canal project that is flooding much of the Oklawaha River basin causing what scientists say are disastrous ecological changes.[1]

There are suits to keep the U.S. Forest Service from allowing Walt Disney Productions to build a commercial resort at Mineral King in the Sierra Nevada. Anti-trust charges are being brought against major auto manufacturers for an alleged conspiracy not to compete in the development of exhaust control devices. Damage suits are being brought by the State of New York, two Chicago Aldermen and Los Angeles County. Scientists and other academicians figure importantly in many pending actions in part because they are strongly represented in the membership groups such as the Sierra Club which is bringing suits and in part because they often testify as expert witnesses.

Lawyers and law school professors are becoming aware of conservation law as a potentially important field. This year the American Trial Lawyers Association has established an environmental law committee which is arranging a series of seminars and is planning to establish an environmental law service. For two years now the Environmental Defense Fund (EDF) has been asserting in anti-DDT cases and other actions that people have a constitutional right to clean environment. EDF filed a suit in the Federal Courts in Montana to force the Hoerner Waldorf Paper Company to provide an adequate air pollution control process at its Missoula pulp mill. The mill is responsible for heavy emission of active sulphur compounds that are polluting the regional air shed.

Professor of Law E. F. Roberts from Cornell believes the 9th amendment if interpreted properly can extend constitutional protection to the environment once there is an enunciation of a right to environmental protection. It "would require every agency of government whether a local zoning board or a federal home mortgage lending agency to review their plans to make certain that their activities did not actually exacerbate deterioration of the environment. The question, of course, is hard to reconcile right to environmental protection", with necessities such as carrying on industrial and commercial activities, system of mass transport and building homes for an expanding population.

Another legal doctrine to be invoked is the "Trust Doctrine". This ancient doctrine holds that all land was held in trust for the people by the sovereign or government. The government must according to this doctrine see that no land public or private is abused or otherwise used in ways contrary to the public interest. The doctrine has already been recognized by the courts in certain cases involving submerged land and publicly owned land. Professor of Law, Joseph Sax from University of Michigan views this doctrine as a particularly useful and flexible legal concept. If courts should ever apply the trust doctrine or the 9th amendment argument in a wide variety of environmental cases, this would force the executive and legislative branches to move at a faster pace in setting and enforcing standards for environmental protection. One of the real difficulties is that courts tend to be conservative, act on precedent and are probably behind public opinion with respect to questions of environmental protection.

During the 19th and 20th century courts were the instruments of laissez-faire economies. For example, a Tennessee court in 1904 permitted 2 copper smelting companies to pollute the air with clouds of billowing sulphur dioxide smoke which made a wasteland of the surrounding valley in spite of farmers protests who had to reside in a valley totally polluted with damaging chemicals. However, judicial attitudes are evolving in a variety of matters involving the public interest and social welfare. The private entrepreneur no longer enjoys the freedom of action he once did. Nevertheless Professor Roberts noted that a court recently allowed a cement plant in the Albany neighborhood to continue polluting the air with cement dust provided it gave damages to the residents in the area.

With concern about the environment now widespread it seems likely that the public and most elected officials would support strong court action to curb pollution and other forms of environmental degradation. The "New Conservation" is calling for the rational use of the environment in the interests of a high quality of life. It

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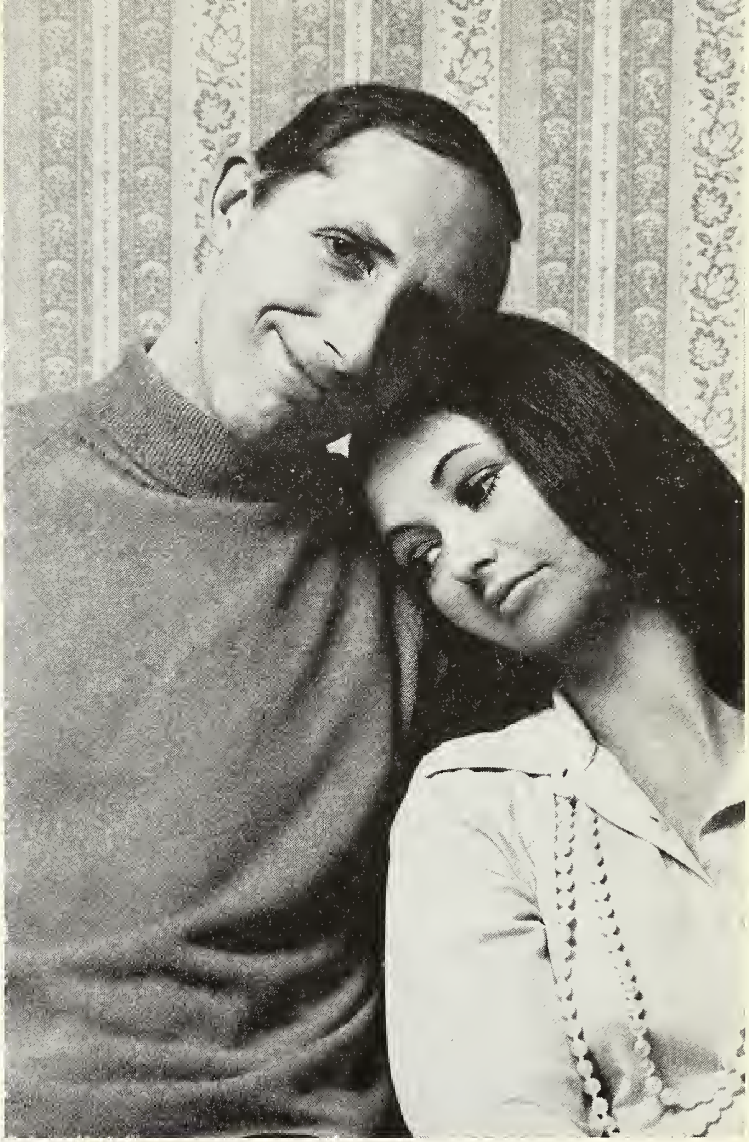

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is as much concerned with the urban environment as it is with wilderness and other natural areas. The conservation movement can no longer be regarded as a "special interest" of concern chiefly to sportsmen wilderness and preservationists. Conservation has a fast growing constituency.

Problems such as noise and air pollution bear especially heavily on low income people who cannot escape from industrial districts and cannot afford air conditioned houses. These people in many cases and their labor unions are becoming increasingly concerned about environmental issues. Political careers will be built on this issue. Bob Eckhardt (D. Texas) was elected to Congress in 1966 because he was a crusader on environmental quality. His constituents suffered daily the odors and eye-smarting fumes emanating from plants along the Houston ship canal. There is also a strong possibility that the conservation and civil rights movements may form an alliance against worsening air pollution, traffic congestions and other problems.

It is time as Oliver Wendell Holmes once said that judges must respond "to the felt necessities of the times". It would seem that the time has come when the courts will begin to play an important role in helping to resolve the environmental crises. Ecology is giving conservation its scientific rationale and scientists are playing a major role in conservation law cases.

L.H.N.

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Medical Science And Practice In The Next Decade

Hindsight is a far more reliable judge of change than is the crystal ball. When Dr. Peart[1] was asked the question of what he thinks the 70's will bring in medicine and medical care, he emphasized that the role of our profession will be to ensure that the quality of medical care is maintained at least at the present levels in the face of a variety of economic and social pressures. Medical knowledge now turns over every 6-8 years and this process may even be accelerated as a result of social pressures that are being applied and the new technology that is growing by leaps and bounds.

We may all agree that there will likely be many changes not only in diagnosis, treatment and rehabilitation of disease, but also in methods of providing these services. There will be an increasingly younger population as well as an older population which will pressure an impatient federal government to enter more actively in the health field than it already has done. Specifically there will result changes in methods of delivery of primary medical care through experimentation. There will probably arise more clinics utilizing allied health personnel to a greater extent than is the case today.

More flexibility in undergraduate and graduate education may be expected with some shortening of medical training. We can expect a concentration on the training of specialists which are in short supply, as for example, ophthalmology. We may expect more coordination of research both within medical education and between various scientific disciplines. Research will probably address itself more in certain areas such as heart disease and cancer. We must all hope for a breakthrough in the rejection process in organ transplant surgery with improved immunology in this field. Hopefully too, there will be a break-through in the cause and prevention of cancer. There will probably be some progress in genetic engineering as it affects the reduction of congenital normalities and abnormalities. We cannot expect an eventual super-race, but we can expect a better utilization of the latent and manifest potential of our infants and young children.

We can foresee the greater use of computers in medicine and health care generally. This should be particularly evident in the hospital field to effect greater economies in administration and in the use of materials and services.

Greater attention will also be paid to low income persons and families both in isolated and urban communities in an effort to improve their living conditions and productivity as well as their health services. Throughout the coming decade there will be more emphasis on the physical fitness at all ages. Health education will encourage our people to accept more responsibility for their individual health. There will probably also develop a movement of more widespread screening for diseases. On the other hand there may very well be an increase in the incidence of mental disease with the increasing tempo of modern life. The frustrations of the young generation will lead many away from facing up to reality and instead retreat to the use of hallucinogenic drugs intoxicants and tranquilizing drugs.

There will be an increased number of accidental deaths in the 1970's as more and and bigger powered cars, motor boats, snowmobiles and airplanes come into use. The fact that we will have more leisure time to use these vehicles for pleasure will be a contributory cause to the increase. On the other hand we may expect a greater amelioration in the presently growing air and water pollution now that the people and their government have become alarmed at the threat to our health and future welfare from continued degradation of our environment.

The 1970's should be an interesting paradox: achievement in medical science and knowledge on the one hand and the creation of more problems in the socio-economic fields on the other. Our profession will have to take an active role in the developing and testing of new methods of medical practice with the view of improving health services. With the government seeking to reduce medical costs, our major responsibility will be to ensure that the quality of medical care does not deteriorate under such pressures..

L.H.N.

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An Institution For Environmental Studies: Redesigning The Environment

There is growing student concern about pollution and other forms of environmental degradation. This concern is shown in widespread movements which are being promoted nationally by a newly chartered tax-exempt organization called Environmental Teach-in, Inc. of which Senator Gaylord Nelson and Representative Paul McCloskey (R-Wis.) are the Co-Chairmen. This organization will help teach-in groups everywhere to plan their own activities. At Michigan the teach-in group is called Environmental Action for Survival (ENACT), a continuing organization that will carry on education and action-oriented activities after the teach-in itself has been held.[1]

The teach-in will be an effort to promote programs of interdisciplinary study of environmental problems; draw public attention to these problems, encourage environment education activities and discuss and carry out action projects. These will include drafting and promoting of legislation, the reporting of pollution-law violators, filing of environmental lawsuits and active campaigns for elective officials who have sound positions on environmental issues. This is a short term approach to a way to treat environment—that is correction of technological errors—meaning pollution control. This short term problem of pollution control is as far as present day public concern goes.

There is also the long term design and control of the environment. The Tukey[2] report of 1965 defines this problem precisely. The report admits that Western industrial societies have made a mess of their own home partly because human beings are apt to be messy, but also because of the over-confident use of technological aids such as pesticides, the profligate overuse of resources like water and the burning of fossil fuels. This has messed up America and threatens to mess up the world. The report makes many sweeping recommendations for action, hardly any of which have been acted upon. Why private interests have been allowed to poison our environment is not spelled out. The student activists might perhaps help here.

The fact is, however, many of the problems defined by the authors in the Tukey report require a kind of knowledge and a type of expert which we have not produced thus far. Perhaps Universities will turn their attention to develop knowledge and train experts with the necessary skills of environmental knowledge and fired with a concern for environmental restoration. The experts will produce theory to solve societal ills as physicians now are trained to solve ills of human beings. Solving immediate environmental ills will be hard enough but it will not be enough. Something altogether more exciting and far reaching will be needed, for in the future we will have to increasingly control and design our environment.

We can extend our horizons with our knowledge for such control from the walls of our house to the end of the earth. It will take time, but we can and must convert the planet into a safer and more comfortable home for our own species and for other living things with whom we can exist and without whom, of course, we could neither eat nor breathe. Boulding[3] argues that economics must enter into the picture if ecology is not to become merely a bird watching and egg-scratching activity. We have to earn our living by seeing to it that the rest of the living world can survive too. This requires a long term and exalted view of our environment. It will require a different view of our priorities and a lot of money to carry it out successfully.

Hare[1] points out four aspects of the concept "environment". One is the material environment which means the physical biotic world outside society and our interactions with it. Another is the social environment arising from the obvious fact that each of us has to survive in a matrix of our fellowmen and that each society must coexist with surrounding societies. This means such problems of the cities and its nightmarish inadequacies. On a world scale it means tensions between countries and between factions within countries. Nearly all the deep-seated political problems of the world reside here. A major function of environmental design must then be to reduce these tensions. A third factor is the built environment—manmade structures that provide a home for mankind and accommodates for his work, play and higher culture. Finally is the total environment.

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In many universities that have launched environmental studies, there is only provision thus far to look after the material environment through the physical and biologic sciences. But a study of the total problem requires something like the following thinking. The study of man's environment natural, social, built, complex is a splendid focus for future academic development. It touches on life and death problems of supporting society and opens up new lines of intellectual experiment.

A unified program of environmental studies must search for the links that in the real world connect man's work and play with the people that surround him, his society, neighboring societies, and human societies at large with the rest of the material world. Our viewpoint, of course, is Western industralized society rather than other societies. Probably the solution of our environmental problems will require some deep seated changes in society itself.

We shall try increasingly to design and build our future environment but for this we will need a better intellectual atmosphere to engage in such conscious creation. Such an endeavor would be for the benefit of all. Then when environmental theory is created it will have to be put into practice and this means political action and the evolution of institutions to cope with new ideas and new requirements. We will not succeed without political scientists taking an active role.

What this all adds up to is that to be really positive and successful, environmental studies ought to involve a large part of a university and spread downward until it contributes heavily to the undergraduate curriculum and influences what is to be done.

L.H.N.

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When To Use A Transvenous Catheter Pacemaker

Heart block of varying degree complicating acute myocardial infarction is usually transient, reversion to sinus rhythm may occur in a few hours or even after one week or more. Among the survivors permanent advanced heart block is infrequent in most reported cases. Paulk and Hurst[1] however, reported 25 per cent incidence of persistent complete heart block. Some have found much lower figures. With the advent of continuous coronary care, monitoring, the incidence of advanced heart block is quite variable from 3 to 16 per cent. In spite of various types of medical treatment available, the mortality rate of advanced block is alarmingly high whereas first degree block does not necessarily worsen the prognosis.

In view of the propensity of patients with advanced block to develop ventricular arrhythmia or standstill and heart failure due to slow ventricular rate, artificial pacing was believed to be of value. Narvas, et al[2] now report on 117 patients monitored during acute MI. They found an incidence of 1st degree block in 4 per cent, 2nd degree in 7 and complete block in 8 per cent. The occurrence of advanced heart block in acute MI generally implies severe disease of the major coronary vessels.

There appears to be a consensus that temporary pacing can be life saving in patients with advanced heart block or with sinus node dysfunction associated with slow ventricular rate complicated by congestive heart failure, Stokes-Adams episodes or multifocal ventricular ectopic beats.[3] In view of the paucity of reports and lack of controlled series, there is still disagreement as to whether or not pacemaker insertion should be the initial treatment of choice. Apparently there is no evidence that pacing can alter the outcome of cardiogenic shock. The various authors who have reported on this subject seem to agree also that pacing may be of benefit in rate related congestive failure and also in preventing recurrences of Stokes-Adams episodes.

In Narvas, et al series[2] catheter pacing was employed in patients with preceding Stokes-Adams syndrome, congestive heart failure and multifocal or frequent ventricular ectopic beats. They recognized the unpredictable effect of isoproterenol and considered catheter pacing as an initial treatment device in advanced heart block regardless of the site of the infarct and QRS duration. They did not feel justified in using catheter pace-maker insertion in asymptomatic patients since the method is not without its hazards. Arterial embolism occurred in two cases. An occasional case will not respond due to bad insertion of catheter. Then there is always the threat of perforation of the right ventricle by the catheter.

It appears that preceding Stokes-Adams episodes, cardiogenic shock and anterior infarction with wide QRS complexes are poor prognostic signs. Six patients without complications and not paced survived (normal QRS duration and rate over 60). Furthermore, the study indicates that prophylactic transvenous catheter insertion in acute heart block does not appear justified unless specific indications arise.

Undoubtedly a normal QRS duration will be of significance only if the heart rate is adequate and the size of the infarct is small. If the QRS duration is normal, but the heart rate is too slow, catheter pacing is still required in the presence of heart failure or the Stokes-Adams syndrome.

Other factors contributing to the increase in mortality and morbidity as experienced by various authors and in some of Narvas, patients include complications related to pacemaker device and consequences of cardiac arrest. Recognized risks are ventricular fibrillation, catheter displacement, myocardial perforation, septicemia and mechanical failure of a defective pacemaker or catheter.

Ventricular fibrillation can occur during intracardiac manipulation and in the presence of competition between the pacemaker beat and the intrinsic cardiac activity if the stimulus falls on the apex of T (vulnerable period). Occasionally it may occur spontaneously. Competition is now best avoided by the use of a demand or standby pacemaker. Myocardial perforation and intracardiac displacement can produce serious consequences if not immediately recognized since either may give rise to intermittent pacing or less effective pacing unless the pacemaker voltage is increased. Cardiac tamponade following myocardial perforation by the catheter appears to be a rare possibility. It is clear a skillful hand and alertness is required once it has been decided to insert a pacemaker.

Complications probably related to cardiac arrest such as aspiration pneumonia, renal shutdown and extensive brain damage have been experienced in various reported series and these certainly contributed to the deaths of some patients. Since the mortality is highest when the infarct is extensive and there are associated complications, Narvas recommends pacing in all cases of advanced block in acute myocardial infarction.

L.H.N.

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Some Complexities Of Small Intestinal Physiology

The small intestine is a complex organ composed of basic functional units comprised of crypts containing dividing cells, of villi made up of highly differentiated cells. The cells of the crypts can be studied by how they incorporate radioactive thymidine into DNA. They divide actively and the cells migrate from the crypts along the length of the villi and complete their life span within 36-48 hours by extrusion from the tips of the villi into the intestinal lumen. There they disintegrate liberating the enzymes needed for digestion of foods. The cells of the crypts are non differentiated whereas the epithelial cells of the villus are highly specialized for the primary intestinal function of digestion and absorption.

The cells of the crypts are arranged in tubules and have a glandular appearance. The villus on the other hand is composed of columnar epithelial cells arranged around an inner core of lamina propria. There is also a junctional zone composed of cells from both crypt and villus. Fortin-Magana, et al[1] studied intestinal enzymes to see whether they arose in the crypt or villus. The submucosa is not in a proliferative state and, therefore, thymidine incorporation is low here. The crypts are actively proliferating cells and the enzyme of thymidine incorporation—thymidine kinase has a very short half life.

Digestive enzymes like lactase are very low in the crypts but reach a maximum in the mid villus and diminish as the tip of the villus is reached. We thus have a constant cycle of cells from the crypt being released, reach the villus and degenerate here to liberate their digestive enzymes into the intestinal tract. The crypts are probably the most actively dividing group of cells in the body.

In addition to digestive enzymes, Said[2] now reports on a new polypeptide they extracted from small intestines which is a highly active vasodepressor. Biologically active polypeptides such as bradykinin and angiotensin are already known to exercise considerable importance in a variety of physiological, pharmacological and pathological conditions. These authors had already extracted from normal lung tissue a peptide fraction capable of causing gradual and prolonged peripheral vasodilation. This finding led them to pursue the search for similar vasoactive principles in extracts of other metabolically active organs.

They assayed the vasoactivity of the different extract fractions from the intestinal tract by measuring the increase in femoral arterial blood flow caused by their infusion at a constant speed into a concentrated branch of a femoral artery of a dog. The infusion of this active extract produced a marked and prolonged increase in femoral blood flow. The onset was much like that of bradykinin but lasted several times as long. The increase in flow was accompanied by a fall in systemic blood pressure by as much as 50 Hg. lasting as long as the increased flow.

If the active peptide was infused in the vena cava it increased the flow in the splanchnic vessels along with lowering the arterial pressure. However, if the active principle was infused into the portal vein, no change in blood pressure occurred suggesting that the peptide is inactivated or removed by the liver. Many years ago Bayliss and Starling also observed a vaso-depresser effect of intestinal extracts. Since then the gut has been shown to contain several vasoactive substances including histamine prostaglandins and now Said's polypeptide.

We now need to find out what effects this systemic vasodilator peptide may have on other vascular beds, for example the pulmonary circulation as well as on other smooth muscle tissues such as the bronchial tree and the digestive tract itself. It also remains to be determined whether this peptide is related to the vasoactive lung peptide. In any case its strong and unusually prolonged vasodilator action on the splanchnic circulation raises the possibility that it might have a physiological role in the regulation of blood flow to the digestive organs.

Release of this peptide could be an important mechanism in the production of systemic hypotension and splanchnic vasodilatation in such conditions as endotoxic shock. It is also reasonable to speculate that if the liver is normally the main site for inactivating this vaso active intestinal peptide, its failure of destruction when liver function is seriously impaired, for example in hepatic cirrhosis, could account for the peripheral vaso-dilation complicating that disease. It might also account for the failure of high concentrations of aldosterone in hepatic disease to lead to hypertension.

What part of the intestinal mucosa is involved in the production of this polypeptide is yet to be investigated.

L.H.N.

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Exercise Training For The Patient With Chronic Obstructive Pulmonary Disease

Chronic obstructive pulmonary disease is a leading cause of both morbidity and mortality in the United States. Emphysema accounts for 7 per cent of disability pensions and together with other bronchopulmonary disorders accounts for almost 2 per cent of annual deaths.[1,2] Bronchopulmonary disorders are numerous and precise diagnosis must be established for proper therapy. Preventive measures such as discontinuance of smoking and proper use of antibiotics to prevent and treat respiratory infections can help to preserve existing function and, of course, mucolytic and expectorant agents help those patients who cough effectively.

Shortness of breath is the symptom which most often brings patients with chronic bronchitis, emphysema and left heart failure to the physician. A sudden increase in symptoms in these patients is often caused by an attack of acute asthma or infection. In fact infection often precipitates bronchial asthma or left heart failure. It is the shortness of breath which limits the activity of such patients and the resultant lack of activity which leads to an unfit state and further increase in dyspnea—a vicious cycle now emerges.

Subjective improvement has been reported by a few advocates of graded exercise training for patients with chronic obstructive pulmonary disease (COPD). Bass et al[3] undertook to analyze the mechanisms of improvement and the possible limiting factors of successful training. They analyzed the results in 12 patients suffering from COPD who exercised seated on a bicycle ergometer. The patients first rested 30 minutes, then exercised against a preselected and constant work load. The patients then carried on the same exercise on a bicycle ergometer at home with instructions to exercise but not exhaust themselves. The patients then returned weekly to the lab for repeat studies.

Eleven completed the study. All had a significant decrease in resting heart rate and 5th minute heart rate. After 18 weeks of this training, the patients exhibited significant decrease in maximum work load. All demonstrated significant increase in respiratory capacity and maximum voluntary ventilation. Other pulmonary function measurements did not change significantly for the group between the initial and 18th week of study. It is possible to claim that the decrease in dyspnea noted was psychological. Indeed exercise can have a positive psychological effect. However, objective measurements of improvement were noted to accompany the subjective claims of these patients.

Increase in the activity of these patients was evident in calculated diary scores which were found to be valuable both by patients and physicians. The patients claimed the diary scores served as an incentive to perform increased amounts of exercise and physicians felt it was a valuable tool to quantify home performance. When a decrease occurred in the weekly diary score, it was often found to be an early sign of intercurrent infection or a clue that the patient had not kept up with his program.

The most sensitive gauge of training and of good health in these patients was the magnitude of decrease in heart rate from the initial level both at rest and during exercise. After achieving the trained state, an increase in the resting heart rate proved to be the harbinger of an acute respiratory infection or of other illness. During the 18 weeks of training none of the patients had a heart rate as high as the preliminary rate even in the presence of an intercurrent illness.

The maximum work load achieved in subsequent visits increased for the 11 patients completing the program. After training interruption of exercise for short intervals there resulted a decrease in the maximal work load achieved at the next laboratory visit. However, the maximal work load never fell as low as the preliminary level.

It is possible to hypothesize that patients with only emphesema or chronic bronchitis improve because of improvement in the chest wall mechanism with a resulting improvement in ventilation/perfusion relationships. All patients completing the exercise program actually did show significant improvement in their respiratory capacity and maximal voluntary ventilation at the 18th week. Other indices of pulmonary function were not significantly altered for the group. However, changes occurring in individual patients helped to quantify the presence and degree of either bronchospasm or left heart failure at the time of each exercise study.[4] Subjective and objective improvement seemed to correlate with motivation of the patient to lead a more active life. The physiologic index easiest to follow and correlating best with improvement after training was heart rate both at rest and during exercise, a lower heart rate indicating a fit state.

One consideration not dealt with by the authors but well known in physiology is the improvement in general muscular efficiency resulting from exercise in which the muscles can do more work with less oxygen requirement thereby reducing the work of the heart.

L.H.N.

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L-Dopa In Parkinsonism

No important development in drug therapy of Parkinsonism has occurred until L-dopa was introduced in this decade. No long term benefits from sterotactic surgery has been confirmed in spite of the initial stereotactic claims. Some causes of the disease are known such as viral toxins, vascular disease and drugs such as phenothiazines and reserpine. However, in most cases no causes can be identified. Pathological examination of the brain in such patients reveals widespread degenerative changes in the basal ganglia particularly the substantia nigra and corpus striatum. Since the same disease results from drugs which deplete tissues of catecholamine and serotonin it was logical to search for the amine which is depleted in Parkinsonism and replace it to determine whether such an approach would be therapeutic.

The Parkinson patient suffers a gross depletion of dopamine in the corpus striatum[1] a similar reduction is found in a major metabolite of dopamine, homovanillic acid. Dopamine probably acts not as precursor of nor-adrenalin, but as a neurotransmitter in the central nervous system and is concerned with mediating inhibition in a negristriatal pathway. The present view is that the therapeutic activity of L-dopa in Parkinsonism results from its conversion to dopamine in the brain. It is obvious that if sufficient neural pathways are destroyed by disease that a neurotransmitter will not restore them and it is to be expected that L-dopa would not be effective in all cases of Parkinsonism.

There are findings which indicate that acetylcholine may be an excitatory transmitter in the striatum. If so then a balance may exist between the activity of acetylcholine and dopamine in the striatum. Drugs which deplete the brain of dopamine or increase the concentration of acetylcholine do exaggerate the symptoms of Parkinsonism. There is an occasional case unresponsive to L-dopa in which a dramatic response can be achieved with 5-hydroxy-tryptophane a precursor of serotoxin. This suggests that sometimes there is a decrease of serotoxin in the brain of affected subjects.

When L-dopa was first evaluated in Parkinsonism both favorable and less favorable results were recorded probably because of small doses and the short periods used. In 1967 Cotzias reported on the use of large oral dozes for periods up to a year by gradually increasing the intake of L-dopa titrating this agent against adverse effects in each patient individually. Dramatic therapeutic results were obtained in 8 out of 16 patients, of whom 4 developed granulocytopenia.

Since then there has been remarkable consistency in the results obtained in different centers. All reports using technics of slowly increasing dosage confirm the general conclusion that in a considerable proportion of patients, L-dopa is a far more potent therapeutic agent than any previously available. The exact reason why some patients fail to benefit is not known. It may be that absorption from the alimentary tract which is normally rapid, differs in such subjects. Pyridoxine is known to antagonize the beneficial effects of L-dopa. But, of course, if nerve tracts are destroyed furnishing a neurotransmitter cannot activate them.

Idiopathic and post-encephalitic patients both respond to L-dopa, so also do those patients whose Parkinson symptoms are due to manganese toxicity. Patients with severe long standing Parkinsonism seem to tolerate L-dopa less well than the mildly affected cases of recent origin although therapeutic successes and failure can occur at every grade of severity. One may expect improvement in at least 50 per cent of the total Parkinson population and in some of these the improvement can be substantial.[2]

The principle clinical feature to improve is hypokinesia. The more obvious and less disabling tremor and rigidity are also alleviated but less consistently. When treatment with L-dopa stops the patients return to their pretreatment status. At present there is insufficient evidence to draw any conclusions as to whether the gradual down hill course of Parkinsonism is modified by L-dopa.

Numerous dose dependent adverse reactions have been reported from the use of L-dopa such as gastro intestinal intolerance, nausea, orthostatic hypotension which can be overcome by slowing the rate of increase of the drug. Other side effects such as dyskinesia and delusions are less easy to manage and may prove so troublesome that treatment has to be abandoned. One aspect of L-dopa recently published, a claim that an increase in libido may be induced, is with-

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out foundation. All adverse effects from L-dopa so far encountered have disappeared where treatment has stopped and there have been no deaths attributed to the drug.

Perhaps the most important point arising from these studies is the realization that striking therapeutic results can be obtained by a new approach to chronic diseases of the nervous system. Previous investigators have focused attention on physiological and pathological abnormalities. It now seems that neurophamacological disturbances ought to receive more emphasis.

Attempts to modulate the action of transmitters in the central nervous system have already achieved some results in psychiatric illness. The therapeutic results currently being obtained in Parkinsonism suggests that similar approaches might be justifiable for other chronic degenerative diseases of the central nervous system once the transmitter substance has been identified in each of these disturbances.

L.H.N.

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Viruses And Cancer: Herpes Virus Vaccine Protects Against Marek's Disease Of Chickens

Herpes Viruses have been found to be etiologic agents in at least two animal cancers so far: Lucke's carcinoma in frogs and Marek's disease in chickens. Lymphomas in cotton-tail rabbits and in monkeys are also caused by herpes virus. There is still some discussion as to whether to consider these diseases as actual cancers. There have also been suggestions of an association between viruses with two human cancers, Burkitt's lymphoma and cancer of the cervix although definite proof is still lacking.

After a herpes virus was isolated from chickens with Marek's disease, further experiments convinced most investigators of its link with the disease. The site of maturation of the virus was found to be the feather follicle epithelium of diseased chickens. The disease typically results in paralysis, enlarged nerves, tumors of many organs and microscopic lesions—lymphocyte infiltration of many structures such as nerves and blood vessels. The infection is spread through the air by other indirect means and nearly all flocks are infected. There is no vertical transmission of virus.

H. G. Purchase has now announced at the Gustav Stern Symposium on Perspectives in Virology held in New York City, the production of a vaccine against Marek's disease prepared from a non-pathogenic turkey herpes virus. It is non-pathogenic for both turkeys and chickens and is isolated from turkey blood, grown in duck embryos and then inoculated in chickens. When these chickens are challenged with Marek's disease virus, they do not develop the disease. Apparently, the resistance is related to antigenic similarities between the turkey virus and Marek's disease virus.

To study the new vaccine, Purchase ran four separate trials that lasted 18.3 weeks. There were four categories of chickens: vaccinated and challenged with virulent virus, vaccinated and unchallenged, unvaccinated and challenged, unvaccinated and unchallenged. Vaccination was carried out at one day of age and challenge with Marek's disease virus between 2-5 weeks of age. The birds vaccinated but unchallenged all showed turkey virus and antibody in their blood. The control birds showed no viruses.

Of the unvaccinated but challenged chickens, 30-70 per cent were dead at the end of the experiment. On the other hand, in the groups that were vaccinated and then challenged, there was complete protection, none died and no microscopic lesions were detected. Of interest is the fact that in about 40 per cent of the vaccinated, challenged chickens, both of the viruses and their antibodies were found to exist simultaneously in the blood stream. Thus many of the vaccinated chickens were infected with Marek's disease virus, but the disease process was halted. This suggests that the mechanism of protection is closer to an interaction between virus and cell or cellular immunity rather than to antibody.

Field trials of vaccine in Michigan and elsewhere are now in progress. Results will be available in about 18 months. No pathogenicity of the turkey virus for chickens has been demonstrated in birds followed over 30 weeks. Dr. Purchase referred also to work on other vaccines against Marek's disease. One developed by Churchill and co-workers in England, is apparently effective, but is made from an attenuated Marek's disease virus.

The vaccine's importance is two-fold. Since the disease is probably due to a herpes virus, the path is cleared for the development of similar vaccines in man if definite proof is found for human viral oncogenesis. It will, of course, also be an economic boon to farmers, who have lost millions of dollars from condemnations of tumorous chickens.

The vaccine certainly is an important development and there should be no procedural difficulties in developing vaccines against herpes viruses in human beings according to Dr. Clyde R. Goodheart of the AMA.

L.H.N.

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The Financial Pinch On Science

The financial problems of health and medical research were intensified early this year by the circumstances surrounding President Nixon's veto of the 1970 Health Appropriations Bill and his signing of a substitute bill. As a consequence health research was pushed back almost to the stringent levels proposed by the administration early last year. Several causes for the decline in federal support for science were offered by Dr. Lee DuBridge.[1] One is the financial demands of the war and now its expansion in Cambodia. Another was the general spending curbs related to the fight on inflation. If these are the reasons that a presidential science adviser believes significant enough to explain the loss of support for research, then the voice of science is receding and it needs a much more effective voice to state its case.

Between 1956 and 1967 the Federal Government increased its support of scientific research from 200 million to 2000 million a year. A growth rate of 21 per cent annually. In the last two years there has been no increase at all which because of inflation actually means a decrease in buying power for research. To scientists especially at Universities the future looks even bleaker because of new restrictions imposed by Congress on the Defense department's support of science not directly related to military needs. In short yesterdays fertilizing flood of government research grants has receded sharply and with it is a mounting discontent and bitterness among American scientists. They are in the midst of prospects halted in mid-investigation; laboratories cannot afford to operate all their expensive equipment; Ph.D's in physics and other fields are dazed to find they are unemployed.

More than a monetary drought helps motivate the spreading alienation and fear of science. To many scientists it looks as though an anti-scientific know-nothing movement is controlling some public opinions. More and more scientists sense fear and dislike of science in the general public and an increasing identification of scientific research with nuclear death, environmental pollution and the population crisis. In this atmosphere many scientists were outraged and hurt to hear a distinguished spokesman for the humanities testifying before Congress and amplifying that over-spending in science may be responsible for the generation gap, distrust between the races and the disappearance of the American consensus. Scientists he demanded "ought to be forced to answer" questions about the impact of their discoveries upon the quality of life" that "humanist" tells the Congressman.[2]

This trend towards viewing a typical scientist as a sort of Dr. Stranglove is very bitter for those affected. It is a complete illusion to think that anyone can map out dangerous areas. The scientist cannot any more than the physicist could when they started studying the atom. A French chemist working on diseases of the silk worm gave us bacteriology. A British bacteriologist gave us penicillin. An obscure Monk in Siberia gave us genetics, potentially dangerous areas from two very old origins. The humanist should have known that the only "safe" research is the research that makes no discovery.

Because of our devotion to science and research this nation and the world have been living through the greatest golden age in the history of science. There is no parallel in history for the explosive quantitative and qualitative advances achieved in the last two decades. Millions of people now alive would have died years ago without the increased power to serve human ends that this unprecedented and grand scientific leap forward has provided. Hundreds of millions now live materially better than their ancestors did.

At the same time astrology flourishes and science research appropriations are cut. Even at the height of *American Science's* public prestige and financial support, the majority of Congressmen and an even greater majority of the voters—whose very lives and welfare is the result of scientific discoveries—had little real understanding of science, its accomplishments, its promise and its limitations.

What is modern science all about? Where are its accomplishments in the last two decades? What new problems have arisen as in the case of our environmental degradation because of the growth of the population and the application and misapplication of modern technology? What have scientists been doing in studying the heavens, the earth, the oceans, living organisms and the mechanism of life itself? All this is found in a collection of books containing articles published in the *Scientific American.*[3]

Molecular biology is the start of the collection as it is of modern science, laboratory breakthroughs by which the double helix of DNA was discovered, the genetic code broken and the stage probably set for man to become master of the biological world as he is of the inanimate world around him. In physics there has been vast progress in probing the atomic nucleus. There is historic achievement in synthesizing DNA and solving the secret of the three dimensional composition and conformation of the aminoacids in hemoglobin and myoglobin.

If those who would now disparge science on humanistic grounds or because of disappointment that science has not solved all problems would take the time to get the birds eye view of the golden age that these volumes afford, they might think more realistically of Science. The fact is scientists are really allies of all who want a better America dedicated to peace, justice for all its people and an environment fit for man now, tomorrow, and for all time. Scientists like all knowledgeable people realize that all new knowledge can be dangerous if misused but that ignorance is still more dangerous.

L.H.N.

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Role Of Catecholamines

(*Nature*, 224: 946, December 6, 1969) It is now possible to measure catecholamines in serum. After myocardial infarction there is significantly more noradrenalin in the serum but not adrenalin. However, in conditions leading to anxiety alone such as cardiac catheterization then it is the adrenalin which increases in the serum not the noradrenalin.

If a complication arises in myocardial infarction, such as pulmonary venous congestion, then very high concentrations of noradrenalin are encountered. A damaged heart is more susceptible than normal hearts are to increased noradrenalin in two ways. In one there is greater tendency to the development of ectopic rhythms. In another, the heart muscle is overstimulated and in presence of an insufficient oxygen supply the cardiac metabolism changes from aerobic to anerobic.

During aerobic metabolism glucose and fatty acids are metabolized. During the anerobic phase considerable amounts of glucose are broken down to lactic acid. Both of these seem to have a deleterious effect on damaged heart muscle.—L.H.N.

Prevention Of Hyperuricemia By Allopurinol In Hypertensive Patients Treated With Chlorothiazide

(*New Eng. J. Medicine*, 282, 133, Jan. 15, 1970, Nicotero, J. A., et al) On a short-term basis a dose of allopurinol 300 mg per day can prevent the hyperuricemia produced by 1.0 gram of chlorothiazide and indeed keep it lower than prethiazide levels.

An impaired uric acid clearance is at least one of the mechanisms for the development of hyperuricemia in the hypertensive patient. Hypertensive patients also exhibit increased concentrations of blood lactic acid which also interfere with the renal excretion of uric acid.

Hyperuricemia is a suspected cause of renal disease and it seems advisable to prevent its induction during therapy of hypertension, especially since hypertensive patients tend to have high uric acid levels.

The hypertensive already carries a heavy therapeutic load with attendant potential for side effects over a long period of treatment. This warrants some hesitation in the prescription of allopurinol as a routine measure in patients who are receiving thiazides.—L.H.N.

Pharmacodynamics of 3, 4-Dihydroxyphenylalanine (Dopa) in Parkinson's Disease

Melvin H. Van Woert, M.D.

Introduction

The use of L-Dopa in the treatment of Parkinson's disease has evolved from the systematic investigation of brain catecholamine metabolism during the last ten years. The aim of this paper is to review the biochemistry and pharmacology of catecholamine metabolism in Parkinson's disease in order to develop a rational understanding of the mechanism of action and mode of administration of L-Dopa. To illustrate some of the side effects, as well as the therapeutic efficacy of L-Dopa, our recent experience with this experimental drug in 34 patients with Parkinson's disease treated at Yale-New Haven Hospital will be briefly described.

Biochemical Considerations

Prior to 1959 little was known of the biochemistry of the extrapyramidal diseases except for the empirical use of atropine-like compounds in the treatment of Parkinson's disease. In 1959, two papers were published describing the distribution of catecholamines in the brain of animals and man.[1,2] Both papers reported that the highest levels of dopamine (see Fig. 1) in the brain were found in the region of the basal ganglia, particularly the putamen and caudate nuclei. It was already known that reserpine, which depletes the brain of dopamine and other catecholamines, induces a parkinsonian-like syndrome in man.[3]

Since Parkinsonism is a disorder of the basal ganglia and reserpine can produce this syndrome, the concentrations of catecholamines in the brains of patients with Parkinson's disease were compared with that of normals. In 1960 Ehringer and Hornykiewicz observed a decrease in dopamine concentrations in the brains of patients who died with Parkinson's disease.[4]. This decrease was most marked in the region of the basal ganglia. Further, the concentrations of norepinephrine,[4] serotonin[4] and homovanillic acid,[5] the major terminal metabolite of dopamine, were also slightly decreased in the parkinsonian brain. A correlary observation is that there is a decrease in urinary dopamine[6] homovanillic acid[7] and spinal fluid homovanillic acid[8] in parkinsonian patients.

The abnormality in dopamine metabolism in Parkinson's disease has been correlated with the neuroanatomy of the extrapyramidal system. In Parkinson's disease the most consistent neuropathological finding is a decrease in the pigmented cells of the *substantia nigra.* The pigment in these cells has been identified as melanin which may be synthesized from catecholamines.[9] With the use of histochemical methods, dopaminergic nerve fibers have been identified that originate in the *substantia nigra* and terminate in the neostriatum.[10]

Recently stereotaxic destruction of the *substantia nigra* in monkeys has produced a biochemical and neurological animal model of Parkinson's disease.[11,12] In monkeys, a *substantia nigra* lesion is associated with a decrease in dopamine and serotonin concentrations in the ipsilateral striatum.[11] Tyrosine hydroxylase (Fig. 1), the rate limiting enzyme in the synthesis of catecholamines, and to a lesser degree dopa decarboxylase are also decreased when the *substantia nigra* is destroyed.[12] The decrease in tyrosine hydroxylase and dopa decarboxylase suggests that dopamine synthesis is impaired by lesions of the *substantia nigra* in monkeys and in parkinsonian patients. We observed that L-phenylalnine, an inhibitor of tyrosine hydroxylase, aggrevated the bradykinesia, rigidity and tremor of Parkinson's disease.[13] This additional evidence supports the hypothesis that there is a defect in dopamine synthesis. The sum of the biochemical evidence suggests that the *substantia nigra* through its nigro-

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This drug is still an experimental drug.

This work was supported by USPHS grant NB 07542 and CA 08341.

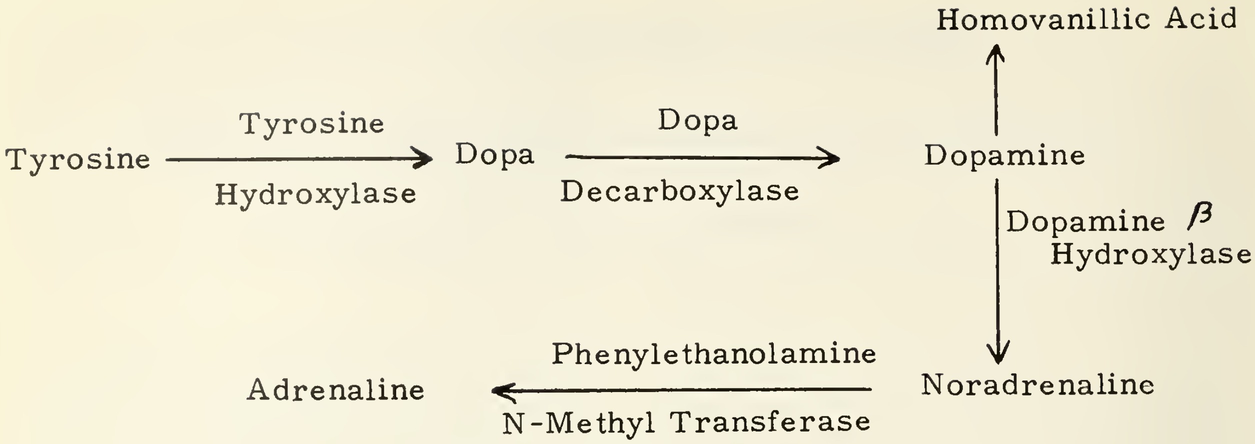

Figure 1

Synthesis of catecholamines from tyrosine.

striatal dopaminergic neurons controls the concentration of dopamine and its synthesis in the basal ganglia. Striatal dopamine probably acts as an inhibitory synaptic neurotransmitter in contradistinction to acetylcholine which has an excitatory action in the basal ganglia. The balance between the excitatory function of acetylcholine and the inhibitory action of dopamine may be impaired in Parkinson's disease due to decreased brain dopamine and by some mechanism this produces tremor and rigidity.

Dopa Therapy of Parkinsonism

Although the mechanism of degeneration of the *substantia nigra* is not known, attempts to increase the dopamine concentration in the striatum of the brain have ensued. Since dopamine does not cross the blood-brain barrier and the conversion of tyrosine to dopa is a very slow reaction, Dopa, the immediate precursor of dopamine has been administered to parkinsonian patients. The first evidence of effectiveness of Dopa in Parkinson's disease was reported in 1961.[14,15] Recent studies using large amounts of oral Dopa have shown the potential usefulness of this drug as a therapeutic agent in Parkinson's disease.[13,16,17] Subsequent therapeutic trials of L-Dopa have confirmed these results.[18,19] However with increased experience and the chronic use of L-Dopa in Parkinson's disease, some of our earlier therapeutic impressions have been modified and the number of toxic side effects have increased. Our experience with 34 parkinsonian patients at Yale New Haven Hospital who since October 1968 have been undergoing treatment with L-Dopa for more than 3 months will be used to illustrate the beneficial and adverse effects of the long term use of L-Dopa. In this study there were 21 men and 13 women who ranged in age from 45 to 86 years. The dose of L-Dopa varied from 2 to 7.5 gm with a mean of 5.0 gm. These patients were all initially hospitalized for 3-4 weeks during which time their standard anti-parkinsonian medications were withdrawn and L-Dopa was administered in gradually increasing doses as tolerated by the individual patient. Their clinical response was monitored by frequent laboratory and daily neurological evaluation in the hospital and outpatient department. The severity of 23 individual neurological signs and symptoms were each rated on a 5 point scale and the results expressed as percentage improvement due to the L-Dopa. As seen in Table 1, the bradykinesia, rigidity and gait were improved to a greater degree by L-Dopa than the tremor. Complete alleviation of their parkinsonian symptoms was seen in 3 patients (8.8%). However two of these patients developed dyskinetic movements of the face and neck as a side reaction to the L-Dopa. Four patients (11.8%) discontinued taking L-Dopa because of gastrointestinal side effects associated with

TABLE 1

EFFECT OF L-DOPA THERAPY ON PARKINSON'S DISEASE

	% Improvement			
	0-25%	26-50%	51-75%	76-100%
Bradykinesia	4	7	12	11
Rigidity	5	8	10	11
Tremor*	9	9	5	6
Gait	5	9	12	8

Two patients had postencephalitic Parkinson's disease, the remainder had the idiopathic type. The duration of Parkinson's disease ranged from 2 to 25 years with a mean of 9.7 years. 5 patients had bilateral thalamotomy and 3 patients had unilateral thalamotomy.

* Tremor was not present in 5 patients.

minimal or no clinical improvement and psychic disturbances necessitated stopping L-Dopa in another patient (2.9%). The remainder of the patients showed significant improvement ranging from minimal (5 patients, 14.7%), moderate (9 patients, 23.5%) to marked (12 patients, 35.3%). Despite complete reversal of bradykinesia, festination and tremor with L-Dopa in some patients, severe emotional stress frequently precipitated a temporary return of these symptoms. L-Dopa also had beneficial effects on other manifestations of Parkinson's disease such as seborrhea, sialorrhea, speech, handwriting, facial expression and posture. There was no apparent difference in response to L-Dopa in those patients who had thalamotomies compared with those who did not have surgery. However, dysarthria and muscle weakness secondary to thalamotomy did not respond to L-Dopa administration. Most of the patients developed further improvement up to 3-4 months after being maintained on the optimal dose of L-Dopa. After an optimal dose of L-Dopa was established during hospitalization, a downward adjustment of dose was frequently necessary during the next 2-6 months due to the development of side effects. Only two patients noted a partial return of bradykinesia and festination after several months of L-Dopa therapy.

Psychic Effects of L-Dopa

In addition to the beneficial effects of L-Dopa on the motor function of parkinsonian patients, there was a definite improvement in mental behavior in some of these patients. The most dramatic changes in mental behavior were noted in three patients who also had senile dementia. These patients became more talkative, their memory improved, they were more alert and aware of their surroundings. They became more interested in their environment and actively participated in conversation. One of the patients who had frequent nightmares and became mentally confused and disoriented at night, noted a disappearance of these symptoms while on L-Dopa therapy. We have initiated a clinical study of the therapeutic effect of L-Dopa on non-parkinsonian patients with senile dementia and Alzheimer's disease. However in three patients with senile dementia and 1 patient with Alzheimer's disease who received a daily dose of 4 and 6 gm of L-Dopa respectively, the clinical and psychiatric evaluation demonstrated no beneficial change in any of the four patients. Mental agitation developed in the three patients with senile dementia.[20]

Two parkinsonian patients who had severe mental depression requiring psychiatric and tricyclic antidepressant therapy showed significant improvement while on L-Dopa therapy. One patient had attempted suicide 2 months prior to his admission to the hospital. The tricyclic antidepressants were discontinued in both patients prior to L-Dopa administration. One patient became more alert, optimistic and assertive on a daily dose of 6 gm of L-dopa which has been sustained over a year. The other patient who was withdrawn, apathetic and self depreciative with suicidal ideation developed a diurnal variation in mood, becoming more cheerful, active, smiling, talking more frequently and rapidly in the late afternoon after receiving a total of 60% of her daily dose. In the morning there was a partial return of her depressive mental symptoms.

Indirect neuropharmacologic evidence suggests that some forms of depression are associated with a relative deficiency of functional brain catecholamines. The monoamine oxidase inhibitors and tricyclic antidepressants increase effective brain catecholamines and relieve depression. L-Dopa can reverse the reserpine induced mental depression in both animals and man.[21] We are presently evaluating the therapeutic effectiveness of L-Dopa in mental depression in patients without Parkinson's disease.

Adverse psychic manifestations were also encountered (Table 2). Three patients developed insomnia and increased dreaming later followed by hallucinations and delusions; these disappeared within 24 hours after the dose of L-Dopa was decreased.

TABLE 2

SIDE EFFECTS (34 PATIENTS)	
Anorexia	16
Nausea and vomiting	18
Heartburn	4
Disagreeable taste	3
Postural hypotension	9
Lightheadedness	8
Dyskinesias	12
Insomnia	8
Increased libido	7
Headache	3
Hallucinations and delusions	5
Anxiety and agitation	5
Rapid speech	2
Lethargy and Somnolence	4
Facial flushing	4

In one case L-Dopa had to be permanently discontinued because of recurrence of these adverse psychic symptoms when L-Dopa was restarted.

When a daily dose of 6 gm of L-Dopa was reached this patient developed insomnia, hyperactivity and talked incessantly and more rapidly than usual. Within 24 hours these symptoms progressed to extreme mental agitation, delusions, paranoid behavior and belligerency eventually requiring physical restraints. He reverted to normal behavior approximately 36 hours after L-Dopa was discontinued. In 3 subsequent attempts to treat with L-Dopa, his psychotic mania-like symptoms returned within 24 hours after a dose of 2 gm of L-Dopa was reached. Each time his motor and mental status reverted to its pretreatment state when L-Dopa was discontinued. It is of interest that the adverse psychiatric symptoms such as hallucinations, delusions and paranoid behavior were not observed in our patients treated with D, L-Dopa.[13]

Other Side Effects

Most patients at some time have one or more side reactions from L-Dopa. Anorexia, nausea and vomiting were the most common toxic effects but subsided spontaneously in some patients without decreasing the dose.. Postural hypotension was frequently observed but was not incapacitating and did not require therapy in any of the patients. Another common and disturbing side effects is the induction of abnormal involuntary movements by L-Dopa. The involuntary movements consisted of dyskinesia of the muscles and tongue, face and upper extremities characterized most commonly by grimacing, chewing and constant irregular movements of the tongue. The intensity of the involuntary movements was directly proportional to the dose. Cardiac arrythmias have been reported by other investigators[16] but were not seen in this study.

Biochemical Changes

Since L-Dopa must be administered in large quantities and probably indefinitely it is likely that L-Dopa or its metabolites may interfere with normal metabolic pathways and impede normal catecholamine synthesis, storage and turn over. Many of the side effects (Table 2) may be due to these biochemical changes.

Although the CSF homovanillic acid (HVA) levels are decreased in Parkinson's disease we have noted a mean 18 fold increase in CSF HVA in our patients treated with L-Dopa.[22] This is an 8 fold increase above the normal control patients' CSF HVA. Therefore L-Dopa treatment of Parkinson's disease not only repletes brain dopamine but actually deluges the brain with dopamine and its metabolites. This excess may explain several of the side effects listed in Table 2. Apparently the nausea, vomiting and oral dyskinesias are due to increased brain dopamine since these symptoms may be induced in animals by dopaminergic nerve stimulation.[23] L-Dopa also decreases brain 5-hydroxyindoleacetic acid, the major metabolite of serotoin. Like L-Dopa, p-chlorophenylalanine, another inhibitor of sereotonin synthesis, can also produce increased libido and psychic disturbances. Thus, the decrease in brain serotonin synthesis associated with L-Dopa therapy may be etiologically related to these side effects.

Plasma tyrosine decreased slightly during L-Dopa therapy but CSF tyrosine levels did not change.[22]

Transient elevations of blood urea nitrogen and SGOT during L-Dopa treatment were observed in 6 and 5 patients respectively. Elevated blood uric acid was seen in 12 of the 34 patients but this may be due to the L-Dopa interfering with the colorimetric method of uric acid determination.[24] Two patients developed a positive direct Coombs test without hemolysis.

Some of the side effects of L-Dopa therapy suggest that the increased synthesis of dopamine may produce hyperactivity of some adrenergic nerve pathways (eg cardiac arrhythmias) or interfere with other adrenergic nerves impeding catecholamine storage or acting as a false neurotransmitter (eg postural hypotension). We have investigated in some detail the effects of L-Dopa and dopamine on pupillary dilation.[25] Pupillary dilation was seen in many of the patients when the daily dose of L-Dopa was 4 gm or higher. In a patient with postganglionic Horner's syndrome, oral dopa and topical dopamine produced dilation only in the normal pupil suggesting that dopamine does not directly stimulate the α receptor of pupillary muscle. The pupillary dilation presumably requires the synthesis of increased amounts of norepinephrine at intact nerve endings. A similar mechanism may occur at other sites in the sympathetic nervous system.

General Principles of L-Dopa Therapy

During the last two years L-Dopa has been used in numerous clinical trials in thousands of patients. As the release of the drug for general use becomes imminent it is timely to review some of the principles of administration that have evolved.

(1) L-Dopa should be administered in gradually increasing daily divided doses to reduce the incidence of nausea and vomiting. Nausea and vomiting are also minimized by administering the L-Dopa immediately after a meal or snack. After an initial

dose of 250 mg three times a day, the daily dose of L-Dopa can be increased 500 mg every 3-4 days until untoward symptoms are encountered or to a maximum of 8 gm per day. The initial administration of the drug is most conveniently and safely administered in the hospital. Like digitalis, the optimum dose varies in each patient and must be carefully titrated according to clinical response. That dose which induces minimal toxicity (dyskinesia, anorexia, agitation, postural hypotension) and maximal improvement is the optimal dose and may vary from 2 to 8 gm.

(2) A therapeutic trial of L-Dopa should continue for at least 4 months since the maximum therapeutic benefit may not be evident before this time.

(3) Patients with bradykinesia and rigidity usually respond better than those with marked tremor.

(4) The duration, severity and etiology of the Parkinson's disease or prior thalamotomy have no apparent relationship to the therapeutic response to L-Dopa.

(5) Laboratory abnormalities which have occured with L-Dopa administration include: elevated blood urea nitrogen, SGOT, uric acid, leukopenia and positive direct Coombs test.

(6) Insomnia, increased dreaming, and agitation may precede more serious mental changes such as delusions, hallucinations and paranoid behavior. The presence of the former symptoms should prompt careful supervision and reduction in dose of L-Dopa.

(7) At the present time L-Dopa should not be administered to patients with cardiac arrythmias, congestive heart failure, recent myocardial infarction or narrow angle glaucoma.

(8) Monoamine oxidase inhibitors, amphetamines and phenothiazines should be discontinued before administering L-Dopa.

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Vaginal Antibiotic For Surgery

Bacterial Evaluation of the Effect of *Furacin Vaginal Suppositories in Relation to Morbidity Following Major Vaginal Surgery

Burton H. Cohen, M.D. and Philip Di Saia, M.D.

The morbidity following vaginal hysterectomy has been reported to vary between 13% to 74%[1-8] depending to a great extent on the criteria utilized. Where these criteria are exacting, it is generally considered that total morbidity following vaginal hysterectomy is higher than following abdominal hysterectomy.[8,17] The bulk of this morbidity are complications which result in infection of the vaginal cuff, pelvis or urinary tract, presumably secondary to operating through a contaminated vagina. An attempt was thus made to reduce the bacteria in the vagina in order to create a less contaminated operative field and hopefully promote healing free of infection.

Methods and Materials

A total of 50 patients were studied. The patients were divided into three categories: Group A—Control group consisting of 19 patients. Group B—pre-operative treatment of the vagina with Nitrofurazone (Furacin®) *suppositories. Fifteen patients were in this group. Group C—pre-operative vaginal preparation with Nitrofurazone, then supplementary therapy with same suppositories during the immediate 7-day post-operative period. Sixteen patients were in this group. Only patients having major gynecologic surgery by the vaginal route with violation of the peritoneal cavity were studied. 85% had associated colporrhaphies performed. Patients were all derived from the Yale-New Haven Hospital Women's Clinic population and all surgery was performed by the resident staff. There was no selection of patients other than the elimination of those who were not diligent in the adherence to the pre-operative regimen. Each patient was given twelve 2 gram Furacin suppositories for vaginal insertion twice daily during the six days immediately preceeding surgery. The nursing staff attended to the insertion of 2 gram suppositories twice daily in those patients designated to receive the post operative Furacin. Detailed bacteriological studies of the vagina and bladder were carried out on all patients prior to, during and after therapy with Furacin. Vaginal cultures, and clean catch urine cultures were obtained in the clinic by the resident staff prior to Furacin therapy, and at the completion of the pre-operative therapy just prior to surgery. Post operative cultures were also obtained on the fifth day from the vagina and bladder, the only difference being that the urine cultures were taken via the indwelling Foley catheter in most cases. Colony counts were the method by which the bacteria were quantitated in the urine.

Morbidity was strictly defined as 1) any temperature elevation greater than 101 degrees Fahrenheit orally or any rise greater than 100 degrees Fahrenheit orally occurring on two consecutive days, 2) any urine culture with a colony count greater than 100,000 colonies/ml, 3) any purulent vaginal discharge associated with pelvic or suprapubic tenderness and 4) the clinical impression by palpation of a cuff abscess or moderate to severe pelvic cellulitis.

Results

A. Change in Flora

Table 1 (A-C) summarizes the results of all vaginal cultures taken in the study. It illustrates nicely changes in flora secondary to surgery and treatment.

B. General Morbidity

In the Control Group A of 19 patients, 18 of whom underwent vaginal hysterectomy with anterior-posterior colporrhaphy, the uncorrected morbidity rate was 79%. If pulmonary complications are eliminated, the corrected morbidity directly referrable to the operative field was 68.4%. Urinary infection was found in 47%, while pelvic infection of some sort was present in 42%. In the group of

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* *Furacin: Eaton Laboratories, Norwich, New York.*

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* *Supported by a Grant from Eaton Laboratories.*

TABLE 1A

CHANGES IN VAGINAL FLORA, GROUP A

Group A

Organism	*Before Surgery*	*After Surgery*
Lactobacilli	9	4
Diphtheroids	8	3
E. Coli	9	17
Enterococcus	8	9
Microaerophilic Strep	4	1
Staph Albus	1	0
Yeast	3	0
Alpha Hem. Strep	4	4
Beta Hem. Strep	0	3
Hem. Staph Aureus	1	3
Proteus	2	1
Klebsiella	2	5
Hem. Corynebacterium	2	1
Clostridium Welchii	1	2
Pseudomonas	0	0
Micrococcus	3	1

TABLE 1B

CHANGES IN VAGINAL FLORA, GROUP B

Group B

Organism	*Before Furacin*	*After Furacin Pre-Op*	*After Surgery*
Lactobacilli	8	4	1
Diphtheroids	9	1	0
E. Coli	4	13	11
Enterococcus	8	9	6
Microaerophilic Strep	3	4	2
Staph Albus	7	0	0
Yeast	3	2	0
Alpha Hem. Strep	1	1	0
Beta Hem. Strep	1	0	0
Hem. Staph Aureus	1	4	1
Proteus	1	1	2
Klebsiella	2	4	1
Hem. Coryebacterium	0	1	0
Clostridium Welchii	0	0	1
Pseudomonas	1	0	0
Micrococcus	0	1	0

TABLE 1C

CHANGES IN VAGINAL FLORA, GROUP C

Group C

Organism	*Before Furacin*	*After Furacin Pre-Op*	*After Surgery and Furacin*
Lactobacilli	12	9	6
Diphtheroids	7	7	4
E. Coli	5	9	11
Enterococcus	5	7	5
Microaerophilic Strep	0	4	3
Staph Albus	0	1	0
Yeast	1	3	1
Alpha Hem. Strep	0	2	0
Beta Hem. Strep	2	0	0
Hem. Staph Aureus	1	0	0
Proteus	1	0	0
Klebsiella	1	4	2
Hem. Corynebacterium	0	1	0
Clostridium Welchii	0	1	0
Pseudomonas	0	0	0
Micrococcus	0	1	0

15 patients treated only with pre-operative Furacin vaginal suppositories (Group B), al lof whom underwent vaginal hysterectomy with anterior-posterior colporrhaphy, the morbidity was not significantly altered (Table 2). Positive urine culture remained with the highest incidence but pelvic infection was diagnosed in 46%. In the group of 16 patients treated pre and post-operatively (Group C), there was little change in the overall morbidity (81%); yet the number of pelvic infections diagnosed was reduced to 25%, approximately half that found in the previous groups. Positive urine culture was

TABLE 2

COMPARATIVE MORBIDITY RATES FOR ALL GROUPS

Morbidity	*Group A*	*Group B*	*Group C*
Pelvic Infection	7 (42%)	7 (46%)	4 (25%)
Postive Urine Culture	9 (47%)	8 (54%)	9 (58%)
Pulmonary	2 (10.5%)	0	0
Thrombophlebitis	1 (5%)	0	0
None	4 (21%)	0	3 (19%)
Average Hospital Stay	8.8 days	7.5 days	9.2 days

found in 58% of this group. As seen in Table 2, the average hospital stay was not significantly altered in any of the groups.

C. Pelvic infections

Seven of nineteen patients in Control Group A developed what was considered clinically a cuff infection. Enteric organisms were cultured from vaginal discharge. E. Coli was found in significant numbers in all seven, Clostridium Welchii in two and enterococcus in five. Normal flora was present in four of these patients in conjunction with the pathogens. Although E. Coli was the most consistent organism cultured, five of these seven patients did not show E. Coli pre-operatively. Seven vaginal cuff infections developed among Group B patients. Again, coliforms were the causative agents, E. Coli was cultured in six of these seven patients. None of these six patients had E. Coli present in the vaginal flora prior to the pre-operative treatment. Four patients in Group C developed cuff infection, and again E. Coli was the primary pathogen culture from all four. Three of these patients were free of E. Coli prior to the pre-operative course of Furacin. Normal flora was present in conjunction with the pathogen in one (1) patient in each of the latter groups.

D. Urinary Tract Infection

Post-operative urine and vaginal cultures were taken simultaneously on the 3-6 post-operative day. Correlation of the vaginal flora with positive urine cultures was made in each group and listed in tables 3A, 3B and 3C. Urine cultures in all patients in the study were sterile pre-operatively. In Group A, nine patients developed a positive urine culture post-operatively. In every case, the causative organism was coliform, and in every case, the same organism was concomitantly cultured from the vagina.

TABLE 3A

CORRELATION OF URINARY PATHOGENS AND VAGINAL CULTURES IN GROUP A

Pt.	*Urine Culture*	*Vaginal Culture*
1	E. Coli, Proteus	E. Coli
2	E. Coli	Enterococcus, E. Coli
3	Enterococcus	Enterococcus
4	Hem Staph Albus. E Colli	Normal flora, E. Coli
5	Klebsiella, Enterococcus	Enterococcus, Klebsiella, E. Coli
6	Enterococcus	E. Coli, Enterococcus, Normal flora
7	Enterococcus	Enterococcus, E. Coli
8	E. Coli	E. Coli, Normal flora
9	E. Coli	E. Coli, Normal flora

TABLE 3B

CORRELATION OF URINARY PATHOGENS AND VAGINAL CULTURES IN GROUP B

Pt.	*Urine Culture*	*Vaginal Culture*
1	E. Coli, Paracolon, Enterococcus	E. Coli, Paracolon, Proteus, Enterococcus
2	Klebsiella	E. Coli, Klebsiella
3	E. Coli	E. Coli, Microaerophilic Strep, Lactobacillus
4	E. Coli	E. Coli, Normal flora
5	Enterococcus	E. Coli, Enterococcus
6	Enterococcus	Enterococcus
7	Proteus	Proteus, E. Coli
8	Proteus	Proteus, E. Coli

TABLE 3C

CORRELATION OF URINARY PATHOGENS AND VAGINAL CULTURES IN GROUP C

Pt.	*Urine Culture*	*Vaginal Culture*
1	E. Coli	Normal Flora, E. Coli
2	Klebsiella	Normal Flora, Kelbsiella, Microaerophilic Strep
3	Enterococcus	Normal Flora, Proteus, E. Coli
4	E. Coli	Normal Flora, E. Coli, Enterococcus
5	Proteus	Normal Flora, E. Coli
6	E. Coli	E. Coli
7	E. Coli	E. Coli, Diphtheroids, Lactobacilli
8	Proteus	Klebsiella, Yeast
9	E. Coli	Proteus, E. Coli

Discussion

The number of patients in each group was small, but detailed bacteriologic studies were performed on each patient. Therefore, this should be considered a pilot study. However, definite trends are apparent and some conclusions can be suggested.

It has been documented by others that the vaginal flora is extremely variable, and even subject to changes over short periods.[9] Normal non-pathogenic vaginal flora often co-exists with pathogens.[9,10] The four most common organisms found were Lactobacilli, Diphtheroids, E. Coli and enterococcus. The pathogens were often found along with small numbers of a variety of non-pathogens called "normal flora" by the laboratory. For this and other reasons, the strict use of normal flora as an indicator of a healthy vaginal environment can easily be misleading. Table 1 shows that operation alone depresses the incidence of non-pathogenic organisms and increases the count of pathogenic enteric organisms. A standard Betadine®* vaginal prep was used on all these cases in the Operating Room just prior to surgery and certainly has an influence in this regard. Interestingly, four of the seven patients in Group A, the untreated group, who developed a cuff infection had normal flora still cohabitating with the offending pathogen. Table 1 further illustrates that Furacin applied to the vagina pre-operatively has a similar effect of depressing non-pathogenic organisms and encouraging the emergence of pathogenic coliforms, although no adverse effect was seen on the morbidity rates. Pelvic infection occurred in 42% of the Control Group and 46% who were treated with Furacin prior to surgery. However, when the prophylactic use of Nitrofurazone was continued in the post-operative period, the incidence of pelvic infection was reduced to 25%. One is unable to account for this on the basis of bacterial studies, as 14 of the 16 patients in Group C cultured enteric organisms in the post-operative period even at the completion of the Furacin course. As in the other groups, here too E. Coli was the most common organism where infection was found. It has been shown[11] that when E. Coli is found in the vagina, it represents a pathogenic strain 86% of the time.

Three conclusions are suggested from this data. First, Furacin vaginal suppositories used pre-operatively appear to alter the normal flora favoring the growth of pathogenic enteric organisms but this did not have an adverse or beneficial effect on the subsequent development of pelvic infection post-operatively. Secondly, the beneficial effect of Furacin suppositories in the post-operative period, as suggested by the lower rate of pelvic infection, cannot be accounted for on a bacteriologic basis. Hemostasis at the conclusion of surgery as well as other factors play a major role in the causation of pelvic infection following vaginal surgery and we are left with the conclusions that the patients in Group C were favored in these respects unknowingly.

Previous studies have shown impressive results in reducing post-operative morbidity with the use of pre-operative antibiotic suppositories.[13-16] Most of these were done in the early 1950's and utilized penicillin and streptomycin. However, the topical use of these preparations is no longer acceptable due to high absorption rates through the mucus membrane and the 1-6% incidence of sensitization.[17] Others have used sulfa preparations and found an initial reduction in morbidity, but after 1½ years of routine pre-op use, the morbidity rose to previous levels.[11] Grimes and Geiger in 1960 reported a decrease in the overall morbidity by almost 50% when large doses of Furacin suppositories were used in the post-op period.

50% of the entire series of patients in all groups developed a urinary tract infection post-operatively. Other series report this complication at an incidence between 15-30%.[1-8] In this study, any urine culture with a significant colony count was regarded as evidence of infection, regardless of whether the patient had developed clinical signs of pyelonephritis. The fact that almost all patients wore a Foley catheter for four or more days post-operatively made the accurate diagnosis of cystitis impossible. The etiology of post-operative urinary tract infections is usually presumed to be a consequence of the indwelling Foley catheter allowing ascending contamination of an irritated bladder mucosa. Interestingly, this study demonstrates that in 91% of the cases the organism from the urine is identical to the one cultured from the vagina post-operatively. Because of this high correlation of organisms in contiguous structures and considering the proximity to the bladder mucosa that a routine anterior colporrhaphy dissection requires, it may be possible that transmigration of organisms from the vagina to the bladder is more of a factor in the etiology of post-operative urinary infection than previously appreciated.

Conclusions

Attempts to sterilize the vagina have never been successful. As in other areas, the use of prophylactic antibiotics has done little but favor the growth of more virulent pathogens. Whether the increased prevalence of these pathogens will lead to greater morbidity from infection in vaginal surgery has not been demonstrated in this study. On the contrary, the incidence of post-operative pelvic infection was decreased in Group C, where the patient was treated both pre and post-operatively with Furacin vaginal suppositories. The suggestion is presented that urinary tract infection following anterior colporrhaphy may be caused by transmigration of organisms from the operative area. Obviously, there are many variables in this problem of infection following vaginal surgery and scientific evaluation of any form of therapy is at best poor. However, the impression was that prophylactic use of antibiotic vaginal suppositories in the form of Furacin vaginal suppositories did not significantly alter the morbidity from vaginal surgery.

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* *Betadine: Purdue-Frederick, Yonkers, New York.*

Synopsis

The low grade but prominent morbidity rate following vaginal hysterectomy has been attributed to the circumstance where one must operate through the vagina, a contaminated field. The efficacy of reducing this hazard by prophylactic vagina antibiosis, in the form of Furacin® vaginal suppositories was evaluated. Bacteriologic studies of the vaginal flora revealed the emergence of virulent pathogens in impressive numbers following therapy but this could not be correlated with any definitive change in the post-operative morbidity. In general, it can be stated that the prophylactic use of Furacin vaginal suppositories for vaginal surgery did not significantly alter the rate of infection following vaginal surgery.

Drugs

Nitrofurazone	Furacin
Povidone-Iodine	Betadine

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CORONARY ARTERIES—There is no doubt that Harvey realized the role of coronary arteries in the nutrition of the heart, since he wrote, "besides, if the blood could permeate the substance of the septum, or could be imbibed from the ventricles, what use were there for the coronary artery and vein, branches of which proceed to the septum itself, to supply it with nourishments." . . . At the close of the sixteenth century the heart was still considered the seat of vitality, the source of animal heat, the laboratory of vital spirits and of arterial blood. . . . It was thought that nutrition was supplied by the venous blood, while the arterial blood supplied the tissues with vitality and heat. Thus we have the peculiar situation of two systems of blood vessels, both carrying blood from the periphery but not returning it to the heart. Harvey's findings dispelled these notions. While the source of animal heat was still incorrectly assigned, the orderly flow of blood for the nourishment of the tissues was established and the coronary circulation was recognized as nourishing the heart muscle, including the septum. —Bing, R. J.: "Coronary Circulation and Cardiac Metabolism," in Fisherman, A. P., and Richards, D. W. (eds.): *Circulation of the Blood: Men and Ideas*, New York: Oxford University Press, 1964.

Sacrococcygeal Teratoma of the Fetus Complicating Pregnancy

Vincent Pepe, M.D, Kyum S. Pyun, M.D., and Rolf E. Katzenstein, M.D.

The striking association of congenital fetal malformations with hydramnios and other complications of pregnancy is well known. The relationship between fetal tumors including fetal sacrococcygeal teratomas, and hydramnios and other complications of pregnancy is not clear. There is no systematic study or review available in the literature.

Upon reviewing the recent articles, there are only two cases with clinical data reported of sacrococcygeal teratoma of the fetus complicating pregnancy.[1,2] Two other cases are briefly mentioned by Charles[3] in a paper reporting a case of nasopharyngeal teratoma with tumor deposits in the lung and associated hydramnios. It is probable that fetal sacroccygeal teratomas with associated hydramnios and other complications may occur much more frequently than they appear in the literature.

Because of paucity of cases recorded, this report of a sacrococcygeal teratoma of the fetus associated with hydramnios, premature delivery and preeclampsia is considered of interest and significant value.

Report of Case

This 26 year old white female, gravida 3, para 2 was admitted to the Meriden-Wallingford Hospital on February 19, 1969. Her last menstrual period was August 18, 1968 and estimated date of confinement was May 25, 1969. She had had two normal term deliveries in February, 1964 and June, 1965. Her past medical history was essentially negative.

On December 17, 1968 she weighed 138 pounds with the uterus the size of four months' gestation. Fetal heart tone was normal. On February 4, 1969 the uterus was the size of eight and one-half months' gestation, her body weight being 151 pounds. There was marked edema of both legs. She was started on Naturetin, 5 mg, daily. An abdominal x-ray revealed a single fetus with hydramnios. No evidence of fetal abnormalities could be found.

Subsequently, the edema increased and became generalized despite increased dosage of the diuretic. The patient became quite uncomfortable, developed a toxic facies and orthopnea.

One day prior to admission the patient's weight was 173 pounds, BP: 130/80 and the size of the uterus was beyond term. Induction of labor was contemplated, however, the patient went into spontaneous labor.

On admission, physical examination revealed an apprehensive patient in severe, acute distress with a temperature of 98.4°F; the pulse was 128 and regular; respirations were 24 and BP: 142/84. Her abdomen was huge, with 4+ edema extending from the feet to the abdominal wall. Pelvic examination revealed cephalic presentation with 5.0 cm dilation of the cervical os, 95% effacement and 1+ station. Fetal heart tone was not heard.

The patient's blood type was A. Rh positive. An antibody screen test was negative. Hematocrit was 34.5 vol.%, hemoglobin 11.6 gm% and urinalysis was negative.

The membranes were ruptured artificially and approximately 5000cc of yellowish-brown fluid was obtained. She was then given Pictocin, one minum every twenty minutes, intramuscularly. The cervix was fully dilated approximately twenty-one hours after the onset of the labor, one and one-half hours after the membranes were ruptured.

The fetal head and shoulders were delivered spontaneously, however, there was considerable difficulty in extracting the lower portion of the fetus. Under general anesthesia a median episiotomy was performed. After much difficulty, the fetus was suddenly extracted, in retrospect, tearing the sacrococcygeal mass off. The fetus was dead. The mass and placenta were then delivered without difficulty.

Immediate post partum blood pressure ranged from 150/90 to 160/100 for several hours. The urine was negative for albumin.

The edema lessened with continued drug dosage and the patient was discharged on the fourth post partum day.

Post mortem examination of the infant revealed the following: The infant measured 38.0 cm in length with a body weight of approximately 1,300 grams. The sacrococcygeal mass measured 20 × 18 × 8 cm. and weighed 1,100 grams.

The external surface of the tumor was moderately lobulated and covered with skin that showed areas of hemorrhagic necrosis. (Fig. 1). The cut surfaces revealed scattered, lobulated, gray masses, some being soft and others firm. Scattered cystic structures filled with blood tinged, mucoid material or serous fluid were also present.

The internal portion of the tumor was present in the retroperitoneal space of the pelvis and displaced the rectum and urinary bladder, anteriorly. The urinary bladder was markedly distended with urine. The kidneys showed marked hydronephrosis with hydroureters. The other organs revealed no significant abnormalities.

DR. VINCENT PEPE, Senior Attending in Department of Obstetrics & Gynecology, Meriden-Wallingford Hospital, Meriden, Conn.

DR. KYUM S. PYUN, Assistant Pathologist, Meriden-Wallingford Hospital, Meriden, Conn.; Visiting Instructor in Pathology, Albert Einstein College of Medicine, Bronx, New York.

DR. ROLF E. KATZENSTEIN, Pathologist, Meriden-Wallingford Hospital, Meriden, Conn.; Clinical Associate Professor of Pathology, Yale University School of Medicine, New Haven, Conn.

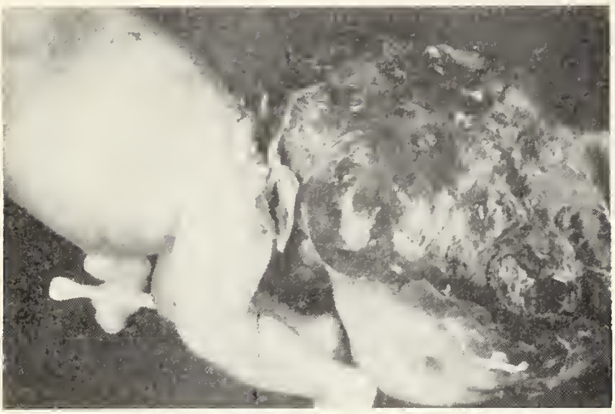

Figure 1
Sacrococcygeal teratoma of the fetus with hemorrhagic necrosis.

Microscopic examination of the tumor revealed all three tissued derived from germ layers. Abundant glial tissue, skin with its appendages, secretory and non-secretory grandular structures, small islands of cartilage, vascular tissue and poorly differentiated mesenchymal tissue were noted.

The placenta was large and edematous. It measured 25 × 20 × 3 cm. and weighed 1,250 grams. No other gross abnormalities were present. Microscopically, the chorionic villi were large with marked edema of the stroma. The capillaries of the villi were scanty and peripherally located. The villi were surrounded by a single epithelium or showed partial persistence of Langhan's layer. The decidual tissue and umbilical cord were not remarkable.

Comment

The pathogenis of the hydramnios is still not clearly understood although many theories have been suggested. In some instances fetal factors such as obstruction of the gastrointestinal tract, absence of the swallowing reflex or obstruction of the respiratory tract appear to play a significant role in producing hydramnios.

Plentle and Grey[4] felt that a metabolic or mechanical pathologic placental change which may embarrass the placental fetal circulation may well be the primary etiological factor on the basis of physio-chemical studies with tracer elements done by the other investigators. Since hydramnios is frequently associated with anomalous development of both placenta and fetus, Prindle & et al[5] stated that both defects are developing concomitantly and are interrelated components of maternal placental fetal disease.

More than 400 cases of the sacrococcygeal variety of teratoma were recorded by 1955.[6] The nature and pathogenesis of these teratomas are unknown. Two prevailing theories are: 1. They represent included twins of the bearer or arise from the bearer's own germ cells. 2. They represent areas of tissue which in embryogenic life escape the action of the organizers and later grow in a disorganized manner.

The manner in which fetal sacrococcygeal teratomas influence the accumulation of large amount of amniotic fluid is not clear, although it too is probably related to a disturbance of the feto-placental circulation.

Summary

A case of hydramnios, premature delivery and preeclampsia complicated by fetal sacrococcygeal teratoma is presented.

It is probable that fetal sacrococcygeal teratomas with associated hydramnios and other complications of pregnancy may occur much more frequently than they appear in the literature although only a few cases have been reported.

The pathogenesis of association between fetal abnormalities and hydramnios is briefly discussed.

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Post-Myocardial-Infarction Syndrome With Anemia

Morton Glasser, M.D.

Introduction (synopsis-abstract)

A complication of acute myocardial infarction, known as Dressler's Syndrome, is characterized by a delayed onset of pericarditis, fever, chest pain, pneumonitis, pleurisy, and a favorable response to steroid therapy.

Anemia has been reported, but only as a late manifestation. To my knowledge, no case of early anemia has been reported. Thus, when considering the above sysptoms accompanied by anemia, we might fail to include this disease in the differential diagnosis since such symptomatology often suggests hemorrhagic pericarditis.

Case History

A 50-year old man entered the hospital with severe anterior chest pain. Acute anterior myocardial infarction was diagnosed by electrocardiogram. SGOT was 400 and LDH 1960 units indicating severe damage. Initial blood pressure was 140/82, pulse 80 and regular. The patient was anticoagulated with Coumadin and prothrombin times kept within therapeutic levels. A pericardial friction rub was heard on the third hospital day, lasted four days, and was associated with a low-grade fever.

The patient did well until the 14th hospital day when he became dyspneic, cyanotic, and complained of chest pain. A pericardial friction rub was heard on the 15th hospital day. Chest x-ray at this time demonstrated enlargement of the cardiac silhouette, bilateral pleural effusion, and patchy bilateral pneumonia. Pulse pressure was low (85/70). His condition worsened in spite of digitalization, diuretics, and oxygen but responded promptly to prednisone therapy. Within 36 hours his temperature returned to normal and respiratory embarrassment subsided. Left-sided thoracentesis yielded 1000 cc. of slightly hemorrhagic fluid.

During the course of prednisone therapy the heart returned to almost normal size (Fig. 2), and the pleural effusions resolved. Prednisone was discontinued on the 27th hospital day. Six days later the patient developed a low-grade fever, left anterior chest pain, left axillary pleuritic pain, hiccups, disorientation, and cardiac silhouette enlargement by x-ray. Prednisone was reinstituted on the 36th hospital day with prompt clinical recovery accompanied by decreased heart size within forty-eight hours. Prednisone was given for the first five months following discharge from the hospital. He has now been without prednisone for ten months.

Anemia was first observed 16 days following admission. Thereafter, this proved to be a consistent finding substantiated on nine different occasions within a month's time. (see Table 1) Repeated stool guaiacs, the direct Coombs' test, antinuclear antibody test, reticulocyte count, L.E. cell preparations were all negative. The patient was not dehydrated during any part of his hospitalization. Within two months of discharge the patient's hemoglobin had risen to 14 gm.% and hematocrit to 43%. It has remained at this level for seven months without the use of iron supplement. This indicates that the original determination of hemoglobin and hematocrit on admission to the hospital was most likely an accurate assessment of the patient's usual red blood cell inventory.

TABLE 1

Hospital Day	*HCT.*	*HGB.*	*WBC*
1st	42%	13.8 gm%	10,300—normal differential normal RBC
16th	30%	9.1 gm%	
17th	31%		
18th	29%		
20th	29%	8.7 9m%	slight hypochromia and anisocytosis
23rd	38%	11.8 gm%	after one unit of packed cells
34th	43%	14 gm%	WBC = 17,700, normal RBC morphology
38th	39%	12.3 gm%	WBC = 10,400, slight hypochromia
45th	36%	11 gm%	
49th	36%	10.6 gm%	

Fifteen months of follow-up since the initial infarction reveals the patient to be in excellent health with normal cardiorespiratory findings.

Although anemia has been reported with protracted cases of post-myocardial-infarction syndrome[1,6] this is the first reported case of an early onset of anemia. The etiology of the anemia is obscure. Although the pleural fluid was slightly bloody, it would not account for the degree of anemia observed in this patient. Certainly the pericardial sac could not hold enough blood to explain a drop in hematocrit from 43% to 29%. Such a sharp drop in red cell volume should therefore dissuade one from diagnosing hemorrhagic pericarditis. This would not be compatible with life. It is

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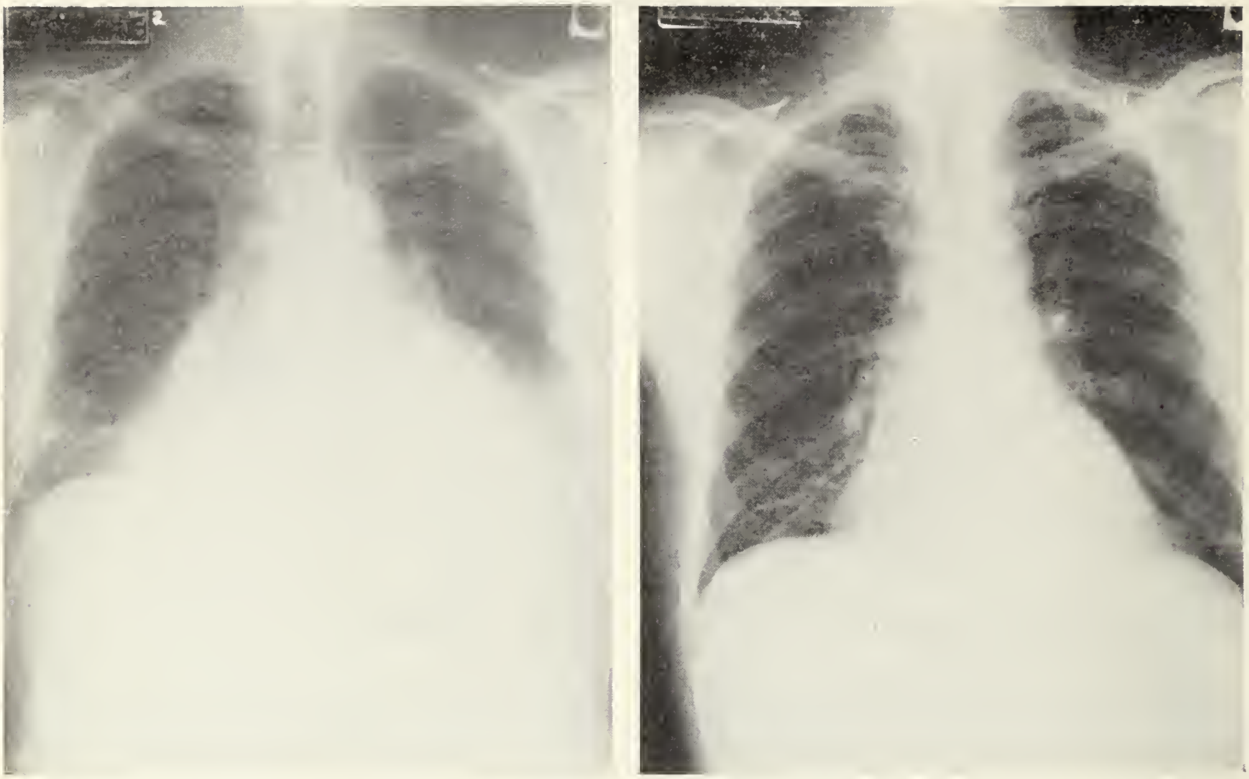
DR. MORTON GLASER, affiliated with Windham Community Memorial Hospital, Willimantic, Conn.

Figure 2



A—Massive cardiac silhouette enlargement and bilateral pulmonary infiltrates before the onset of Prednisone therapy.

B—Return of cardiac silhouette to normal size and resolution of pulmonary infiltrates nine days after the onset of Prednisone therapy.

interesting that the two cases of anemia reported by Dressler also exhibited a hypochromic anemia.

A massive cardiac silhouette accompanied by pericarditis was a striking feature in this case. Pericarditis without effusion is a common occurrence in uncomplicated myocardial infarction. A friction rub is present in 13.8-29 per cent of such cases[3] and is usually heard between the second and fourth days of illness. On the other hand, 80 per cent of Dressler's patients[6] manifested a pericardial friction rub which characteristically appeared at a later date. Sixty-two per cent cent of these were accompanied by effusion.

Hemorrhagic pericarditis[4] may present symptoms similar to those seen in post-myocardial-infarction syndrome: prolonged and recurrent friction rubs, recurrence of cardiac pain, vascular collapse with distended neck veins, low pulse pressure, and pericardial effusion. However, pleural effusions and pneumonitis are not seen with hemorrhagic pericarditis nor has prednisone been reported to be effective in therapy. Both syndromes require the discontinuance of anticoagulants as the first line of therapy. Both may require pericardiocentesis if signs of cardiac tamponade ensue. If it proves impossible to differentiate these two syndromes, an empirical trial of prednisone is justified since its use in Dressler's syndrome is mandatory.

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THE PRESIDENT'S PAGE

The method of delivering medical care is attracting increasing attention and study across the country. While the system of private practice that prevails today has provided high quality medical care, like anything else of high quality, it is expensive. Its critics seem to have stopped calling it a non-system.

There has been an increased demand for medical care created by growing public awareness, by hospital and medical insurance, and by Medicare and Medicaid. This, coupled with a shortage of physicians and their maldistribution is placing a tremendous burden on this system. A change in the method of delivering medical care is being urged by many from different segments of American life. The advocates of other methods claim that their method is better and less expensive.

Among the remedies suggested is a program of National Health Insurance. This is particularly attractive to organized labor, especially if it will be paid for by the employer as a fringe benefit incorporated in the bargaining agreement.

Although a Medicare program had been advocated for many years, its proponents had no plans for its operation. When the Medicare-Medicaid legislation was passed, the Social Security Administration had to scurry around formulating regulations to implement it and no one seemed to know just how it would operate until shortly before it went into effect. Its cost was underestimated in spite of the advice of representatives of organized medicine and its administrators are still promulgating new regulations to cover situations which might have been anticipated. Our experience with Medicare and Medicaid has demonstrated the shortage of manpower and of facilities and the need for study and planning before implementation. Under these circumstances it would be unwise to institute a program of National Health Insurance, which is an extension of Medicare to the rest of the population, before Medicare and Medicaid are operating optimally and the necessary facilities and manpower are available.

Group practice, either prepaid or fee for service, is another method of delivering medical care. Some eighteen year ago while I was a candidate for the Master of Public Health degree at Yale University School of Medicine, I wrote a thesis entitled "The Role of the General Practitioner in the Community". Dr. Ira Hiscock, Chairman of the Department of Public Health, suggested that I visit the HIP prepaid group practice clinic at the Montefiore Hospital in New York. A director of the group assured me that the General Practitioner was a thing of the past and that the future method of delivering medical care would be by prepaid multi-specialty groups. Today it is being said that we need more General Practitioners. It is also interesting to note that Montefiore Hospital recently severed its connection with the HIP group because it was "uneconomic".

The best known examples of prepaid groups are the Kaiser-Permanente groups on the West Coast. In a recent television program a member of one of these groups mentioned a little-known fact, namely, a deterrent or co-insurance feature in the form of a one dollar charge for a clinic visit, and a five dollar charge for a home visit. In addition, those associated with prepaid group clinics readily admit that this type of practice is not acceptable to all doctors nor to all patients. It cannot replace the personal relationship between physician and patient that exists under our present private practice system, and which so many patients and physicians find desirable.

In recruiting physicians for prepaid groups its advocates stress the forty hour week and the rotation of night and weekend work. Dr. Roger Egeberg, the Under Secretary for Health in the Department of Health, Education and Welfare has pointed out that the average doctor now works sixty hours a week and that when he leaves private practice to join a group and works forty hours per week, someone else must take up the slack of the twenty hours he no longer works. The advocates of prepaid group practice do not seem to take this into consideration, when proposing large scale development of this type of delivery of medical care.

In New Haven there are two prepaid group practice programs in the pre-operational stage. The cost to the subscriber has not as yet been announced. Aside from grants for research and study, and outside funds from Foundations that these programs may receive, they will be subsidized by the taxpayers of New Haven in the form of tax-exempt property. One might facetiously speculate how much the cost of medical care might be reduced if the private practitioner were similarly subsidized.

Another form of group practice is the hospital-based group, either prepaid or fee for service. In either case the physician would be a salaried employee of either the hospital or a separate corporation. An advantage is the use of already existing facilities (laboratory, X-ray, etc.). How economic this would be is open to question. As noted above, Montefiore Hospital severed its relationship with a prepaid group because it was "uneconomic". Furthermore, hospital out-patient clinic charges, as calculated on a cost basis, frequently exceed the fees charged by private practitioneers in the same community for similar services.

I have touched only briefly on some of the methods of delivering medical care. I have omitted a discussion of the use of paramedical personnel which is being developed and which I will discuss at a later date.

It is important that we as physicians study and innovate new methods for the delivery of medical care. The Third Party Payments Committee of the Connecticut State Medical Society is studying group practice in Connecticut and also has under consideration the "Foundation" approach to the delivery of medical care suggested by the Hartford County Medical Association Board of Trustees. We must be open-minded and objective about these methods. Because something is new or different does not necessarily mean that it is better than the present system; but it also does not mean that it is worse.

MORRIS A. GRANOFF, M.D.

FROM THE EXECUTIVE DIRECTOR'S OFFICE

William R. Richards, M.D.
Executive Director

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Josephine P. Lindquist
Associate Executive Director

SUMMARY OF ACTIONS COUNCIL MEETING

Thursday, April 23, 1970

I. Attendance

Present in addition to the Chairman, S. J. Martin, and the Vice-Chairman, K. F. Brandon, were: Drs. Granoff, Weber, Jr., Edson, Abbot, Dean, Gardner, Fabro, Grendon, Rogol, Gallo, Harwood, Petrie, Nemoitin, Friedberg, Johnson, McDonald, Pelz, and Root, Jr.

Also present were: Mrs. Lindquist, Mr. Donelan (AMA), Dean Redlich (Yale Medical School), Dean Patterson (UConn Medical School), Mr. Gordon (HCMA), Mr. Olson (FCMA), Dr. M. D. Deren (Committee on Medical Economics and Insurance), Attorney L. Wildman and Dr. Richards.

Absent were: Drs. Polivy, Cramer, Wilson, Jr., Purnell, Roch, Grant, Gorin, von Glahn, Palomba and Klare.

II. Routine Business

Approval of Minutes

As printed and distributed, it was VOTED to approve the minutes of the meeting of March 25, 1970.

Date of Next Meeting

The next meeting of the Council will be held on Wednesday, April 29, 1970.

III. Special Business

Report on Malpractice— Committee on Medical Economics and Insurance

Having reviewed the subject report, receiving the benefit of explanatory remarks by M. David Deren, Committee chairman, and Mr. Wildman, consulting attorney, the Council VOTED to accept the report with gratitude and commendation.

Received for consideration and final action at the next meeting (4/29/70) was a series of recommendations proposed by Dr. Deren

Several actions relating to the report and recommendations were taken as follows:

(a) It was VOTED to authorize M. David Deren, Committee chairman, to explore with Attorney Wildman the development of a plan which would provide the legal services necessary for coordinated implementation by the Society of the several recommendations of the report, and to derive an estimate of the costs of such legal services on a continuing (annual) basis. In addition, Dr. Deren is asked to determine the availability of Attorney Wildman to furnish legislative counselling at the 1970 General Assembly, both as to legislation concerned with malpractice problems and in general.

(b) It was VOTED to authorize Dr. Deren, with Kenneth F. Brandon and J. Alfred Fabro, to explore with responsible insurance carriers (including the Professional Insurance Company) the possibility of developing and marketing a "group" or "quasi-group" malpractice insurance plan for members of the Connecticut State Medical Society which would be in accord with the general recommendations contained in the subject report of the Committee on Medical Economics and Insurance, including possible formal involvement of the Society in the areas of peer review and/or arbitration and the furnishing of experts to testify.

SUMMARY OF ACTIONS COUNCIL MEETING

Wednesday, April 29, 1970

I. Attendance

Present in addition to the Chairman, Dr. S. J. Martin, and the Vice-Chairman, Dr. K. F. Brandon, were: Drs. Granoff, Weber, Jr., Abbot, Dean, Gardner, Fabro, Polivy, Grendon, Rogol, Cramer, Harwood, Petrie, Purnell, Roch, Friedberg, McDonald, Pelz, Root, Jr., Palomba and Klare.

Also present were: Mrs. Lindquist, Mr. Donelan (AMA), Mr. Olson (FSMA), Dr. Deren (Committee on Medical Economics and Insurance), Dr. Hess (Welfare Medical Director) and Dr. Richards.

Absent were: Drs. Edson, Gallo, Wilson, Jr., Grant, Nemoitin, Johnson, Gorin and von Glahn.

II. Routine Business

Approval of Minutes

As printed and distributed, it was VOTED to approve the minutes of the meeting of April 23, 1970.

Life Memberships

It was VOTED to approve applications for Life

Membership received from the following eligible Active Members:

Charles L. Corradino, New Haven (NHCMA)—1970
Jesse S. Harris, New Haven (NHCMA)—1970
Robert Isenman, Westport (FSMA)—1970
R. Harold Lockhart, Fairfield (FCMA)—1971
Paul F. McAlenney, New Haven (NHCMA)—1970
Raymond A. Sterrett, Southport (FCMA)—1971
Eric E. Stietzel, Norwalk (FCMA)—1971
Herman Yannet, Southbury (NHCMA)—1971

Resignations, Appointments, etc.

(a) *Committee on Public Relations*: It was VOTED to accept, with regret, the resignation of Max R. Goldstein, Hartford (Council-nominated on a county basis). It was further VOTED to replace Dr. Goldstein on the slate of nominees for 1970-71 with Harry J. Tamoney, Jr., Hartford, and to so advise the House of Delegates on May 12.

(b) *Conference Committee with Connecticut Pharmaceutical Association*: It was VOTED to accept, with regret, the resignation of Pasquale J. Costa, Jewett City, as a member and the chairman of this Conference Committee (effective May 12, 1970). It was further VOTED to designate Elliott R. Mayo, Waterbury, to serve as chairman of the Committee for 1970-71.

(c) *Editorial Committee of Journal*: It was VOTED to accept, with regret, the resignation of Erwin S. Eskwith, Bridgeport, as a member of the Committee. It was further VOTED to replace Dr. Eskwith on the slate of nominees for 1970-71 with Robert M. Lowman, New Haven, and to so advise the House of Delegates on May 12.

Date of Next Meeting

The next meeting of the Council is to be called by the President "as soon as possible" after the Annual Meeting of the House of Delegates on May 12, 1970. Continuing the current policy of alternating days, a Thursday will be given primary consideration.

III. Old, New and Special Business

Meeting with Insurance Commissioner re Blue Cross

It was VOTED to receive as information a copy of the minutes of a 3/26/70 meeting at the office of Insurance Commissioner Cotter, at which matters relating to Blue Cross rates and hospital costs were discussed jointly by representatives of CSMS, of Blue Cross, of the Hospital Cost Commission and of the Connecticut Hospital Association. Drs. S. J. Martin, C. Polivy and S. L. Cramer participated as representatives of the Society. It was further VOTED to send copies of these minutes to members of the CSMS Committee on Hospitals and that the Committee on Hospitals be requested to review the contents thereof, with Drs. Martin, Polivy, Cramer and perhaps others being invited to participate, and to solicit from the chiefs of staff of the hospitals in Connecticut information as to what is being done in each hospital toward controlling hospital costs.

Meeting with Legislative Subcommittee re Medical Assistance

It was VOTED to receive as information a copy of the minutes of a 3/12/70 meeting of CSMS representatives with Subcommittee III of the General Assembly's Health Care Study Committee at which the Medicaid Program (past, present and future) was jointly discussed. Furnished by the Subcommittee's secretarial staff, the minutes were found to be reasonably accurate insofar as *what* was discussed is concerned but that many of the remarks of the participants, particularly those of the CSMS representatives, were reported in such a manner as to be entirely misleading. Since the Health Care Study Committee is expected to make recommendations to the 1971 General Assembly which are based on these discussions and those held with other groups, it was VOTED to request Drs. Martin, Polivy and Cramer to compose a "corrected" version of the minutes and to distribute same (with staff assistance) to all participants in the March 12 meeting and to the co-chairmen (Senator Schaffer and Rep. Lavery) of the parent Health Care Study Committee.

Activities of Liaison Committee with Welfare Department

Several items of business relating to the activities of the Liaison Committee were considered and acted upon as follows:

(a) It was VOTED to receive as information a 3/13/70 letter from the State's Professional Policy Committee to Charles Polivy, Hartford, Committee chairman, which outlined the plan for payment for physicians' services rendered to Medicaid patients (to become effective July 1, 1970) which the PPC had developed and approved.

(b) It was VOTED to receive as information the minutes of the 3/30/70 meeting of the Liaison Committee at which the payment plan developed and approved by the Professional Policy Committee was reviewed and discussed. In general, the plan was found to accommodate the Society's recommendation that all services be given code numbers and service values in accordance with the CSMS Relative Value Scale, and, to a very limited extent, the Society's recommendation that the payment schedule be "flexible" and reflect the prevailing levels of charges known to obtain in various parts of the state. Provision for duality of payments to generalists vs. specialists was noted, a feature which was abandoned during the pilot "usual and customary charge" program of 3/1/68-3/1/69. Provision is also made to make payment for limited professional services in an emergency room setting and for some "bonus" payments to be made for certain services rendered in the home, in an extended-care facility and in the hospital.

(c) It was VOTED to receive, accept and approve, with minor amendment, a report of the Liaison Committee which recounted its activities during the past year, drew certain conclusions based on its experience, and ended with series of recommendations directed to future activities by the Committee and by the Society. The conclusions and recommendations (as amended) are reproduced below:

CONCLUSIONS:

1. The Liaison Committee by virtue of discussions, study, and meetings, has gained tremendous experience in the field of health costs and health care delivery.
2. The Society's position has been acknowledged by the Professional Policy Committee, and implemented, without having legislative action which indicates that the Professional Policy Committee has the authority to make changes.
3. Payment for professional services in the emergency room will be re-established, separate and distinct from facility charges.
4. Demonstration and realization that peer review is desirable and workable; and controls abuses.
5. It is necessary to present the total Society position worked out well in advance rather than a fragmented individual section approach. Organization is strength.

RECOMMENDATIONS:

1. That the Society continue the activities of the Liaison Committee with the Welfare Department.
2. That the Society gather and maintain up-to-date data as to the performance of individual members and their Sections with regard to the types of services rendered, the methods of delivery of services and the charges made for services.
3. That, to implement No. 2, the Society obtain qualified assistance, such as statisticians, to gather the pertinent data desired, and public relations and legal advice to aid in the Society's contractual relationships with hospitals third party payors and Federal and State agencies.
4. That the Society continue to advocate peer review, through medical advisory committees, as essential to achieving the delivery of uniformly high quality care efficiently at reasonable cost, and to controlling abuses.

On a related matter (attached to the foregoing report) a separate action was taken as follows:

It was VOTED to receive as information a "Minority Opinion" expressing opposition to duality of payments to generalists vs. specialists, filed by Leo F. Giardi, Hartford, who is a member of the Liaison Committee with the Welfare Department. His opposition was directed primarily at the new Medicaid payment schedule, as proposed by the Professional Policy Committee of the State, but applied as well to *any* "fixed fee schedule" offered by *any* third party payor.

Noting that Dr. Giardi's objection would not be applicable to a "usual and customary charge" program, the Council further VOTED to endorse the position held by the American Medical Association on the subject of duality of payments under "fixed" schedules; i.e., that efforts should be made "to reverse such dual fee differentials (where they exist) and to work diligently to prevent the institution thereof (when they are proposed)".

It was further VOTED to transmit this endorsement to the Liaison Committee with the Welfare Department for guidance in its future discussions on Medicaid with the Professional Policy Committee and other State agencies.

Finally, it was VOTED to convey the thanks of the Council to Dr. Polivy and the members of the Liaison Committee for the fine work they have done during the yast year.

Report—Employment of Assistant Executive Directors

Norman H. Gardner, chairman of the Ad Hoc Committee on Administrative Organization and Planning, presented a report to the Council which recounted the Committee's efforts to locate qualified persons to be considered for the post of Assistant Executive Director, the results of interviewing of several candidates, and the conclusions reached by the Committee. In essence, the Committee recommended that two persons be employed (instead of one), one to have the primary designation as Assistant Executive Director for Public Affairs and Socio-Economic Activities, and the other the designation as Assistant Executive Director for Scientific and

Educational Activities. The Council VOTED to approve this recommendation and to authorize the employment of the two persons named by the Committee, their employment to become effective on June 1, 1970. As indicated previously in these minutes, the Council also approved a report of the Fiscal Advisory Committee which recommended the salaries and other benefits of employment to be offered to the two applicants.

Further Consideration—Committee Report on Malpractice

Again joined by M. David Deren, Bridgeport, chairman of the Committee on Medical Economics and Insurance, the council reviewed the series of recommendations offered by Dr. Deren at the meeting of 4/23/70. It appeared to be the conclusion of the majority of Council members that it would be better to have a single new committee study the entire report, and plan for its implementation, rather than to appoint a number of new committees (as originally recommended) whose assigned functions would be more or less indefinite and possibly duplicative. After lengthy discussion, it was VOTED to approve one recommendation only, as follows:

That the Council establish a Committee on Professional Liability to keep pace with developments in the field of malpractice, to coordinate the activities of other committees in their efforts to cope with malpractice problems on behalf of the medical profession in Connecticut, and to initiate and maintain a file on all cases of alleged malpractice (fault or negligence; claim or suit) in Connecticut. The composition of the Committee is to be: A representative of the Council; the chairman of the Committee on Medical Economics and Insurance; the chairman of the Committee on State Legislation; the chairman of the Committee on Public Relations; the chairman of the Committee on Hospitals; the chairman of the Judicial Committee; the chairman of the Conference Committee with the Connecticut Bar Association; and the chairmen of the County Associations' committees that handle malpractice situations (by whatever name). The Committee will be authorized to engage knowledgeable legal counsel, as needed, to advise the Committee and serve as its expert staff.

Based on the report and recommendations of the Committee on Medical Economics, it was further VOTED to approve a suggested listing of activities that the Committee on Professional Liability should engage in, as follows: (a) Conduct an ongoing study of the malpractice problems in Connecticut by soliciting from member physicians the details of malpractice claims and suits brought against them; (b) Conduct an educational program for physicians about malpractice problems and how to avoid them; (c) Refer to the Committee on Public Relations such items as need public dissemination; (d) Refer to the Judicial Committee any instances in which disciplinary action might be indicated; (e) Seek to establish liaison with the State Legislature, the State Bar Association, the State Insurance Commissioner and other interested parties with a view to initiating remedial legislation concerning malpractice; (f) Study the comparative merits of Peer Review vs. Arbitration as mechanisms for handling malpractice claims; (g) Investigate available or to-be-developed plans for a group malpractice insurance coverage program for members of CSMS.

Appointment of Advisory Committee on Anesthesia

The Council considered a request of the Public Health Council, transmitted by the Commissioner of Health, that the Society appoint an Advisory Committee on Anesthesia to advise the Department of Health concerning "problems that occasionally arise about deaths related to the administration of anesthesia in hospitals". In essence the Advisory Committee would conduct confidential reviews of problems in much the same manner as does the Committee on Maternal Morbidity and Mortality. It was VOTED to request the President of the Society, Dr. Martin, to appoint the members of such an Advisory Committee, keeping in mind that not more than one-third of the members should be anesthesiologists and that the remaining two-thirds should be "broadly representative" of different types of practice such as internal medicine, pediatrics, general practice, surgery and pathology. Dr. Martin appointed the Advisory Committee as follows:

William B. Lyons, West Haven—Anesthesiology; Anthony J. Dougherty, Hartford—Anesthesiology; Robert D. Murphy, Wethersfield—Family Practice; Harvey L. Fritz, Meriden—Internal Medicine; John W. Gerster, Greenwich—General Surgery; William E. Hart, Hartford—Pediatrics; and Romeo A. Vidone, Orange—Pathology.

Report—Ad Hoc Committee to Study Abortion

It was VOTED to approve a report filed by the Ad Hoc Committee which recommended that the Society abandon its strictly "medical indication" approach to abortion law reform (House of Delegates, 5/68) and, instead, seek repeal of the existing statutes covering abortion in Connecticut; also, that the Society should seek enactment, under the

Medical Practice Act, of amendments that would provide that abortion may only be carried out by a licensed physician in an accredited hospital. The report adds: "The provision for a 90 day residency requirement for the patient would seem desirable." It was further VOTED to request the Ad Hoc Committee to draw up and submit to the Council for approval a "bill of particulars" for a Society-sponsored bill which would spell out the features (authorizations, contingencies, exclusions, limitations, etc.) which should be included.

Communications—Fairfield County Association

(a) It was VOTED to approve a recommendation of the FCMA Board of Trustees that Alternate Delegates to the American Medical Association be made voting members of the Council, and to introduce an amendment to the Bylaws at the forthcoming annual meeting of the House of Delegates which would accomplish that purpose.

(b) It was VOTED to refer to the Subcommittee to Study and Revise the Bylaws, for study and report, the need and/or desirability of amending the CSMS Bylaws to authorize the admission of qualified doctors of osteopathy into CSMS membership. The FCMA currently has under consideration a FCMA Bylaw amendment which would make qualified osteopaths eligible for County Association (FCMA) membership.

CRMP

(a) It was VOTED to receive as information copies of the minutes of the CRMP Executive Comittee meetings of March 23 and April 13, both furnished by the CRMP office.

(b) It was VOTED to receive as information a letter from Mr. Arthur Rogers, CRMP Advisory Board Chairman, which explained that CRMP has not yet begun its restudy of the High Energy Radiation Therapy Services Program and that its contacts with the Connecticut Division of the American Cancer Society and other agencies are limited to soliciting their participation (through appointed representatives) in the work of the restudy committee when it becomes activated.

(c) It was VOTED to receive as information a series of verbal reports given by Drs. Gardner, Martin, Abbot and Richards about recent activities of CRMP in the fields of program development and implementation. Collectively, the reports indicated that CRMP has developed some 16 new programs (or additions to existing programs) which, it is hoped, will make CRMP eligible to receive $330,000 or more for 1970 under the so-called "challenge award" grant supplement.

(d) It was VOTED to receive, but to defer for consideration until the next Council meeting, a communication from Marvin Garrell, Bridgeport, advising the Council of his personal evaluation of the CUPISS Program (Dr. Garrell serves on the CUPISS Technical Advisory Committee) and making recommendations for CSMS actions concerning same.

N.B.: *The foregoing is a summary of the proceedings and action of the Council on April 23, 1970. Detailed minutes of the meeting are on file at 160 St. Ronan Street, New Haven, for perusal by any interested member of the Society.*

Placement Wanted

NEUROLOGIST—30 years of age, Eligible with National Boards wishes group or associate type practice in Connecticut. Would prefer practice in a multispecialty group preferable with another neurologist.

INTERNIST—30 years of age, Eligible with National Boards wishes solo, group or associate type practice in the south west part of Connecticut. Would consider part or full time hospital practice with some subspecialty work in renal or dialysis medicine. Military obligation will be completed in July, available then.

UROLOGIST—52 years of age, Certified, wishes solo or group type practice in Connecticut. Available immediately.

PATHOLOGIST—34 years of age, Certified with National Boards, wishes associate type practice in Connecticut. Presently in practice.

OB & GYN—32 years of age, Eligible, wishes solo, group or associate type practice in Connecticut. Presently in practice, with Connecticut license.

UROLOGIST—32 years of age, with National Boards, wishes group or associate type practice in Connecticut. Would prefer to go in with at least one other man fairly near a good size hospital. Presently in practice.

PSYCHIATRIST—38 years of age, Eligible with National Boards wishes to practice in Connecticut. Presently in practice. Has done a good deal of in-patient and out-patient work.

INTERNIST-ALLERGY—31 years of age, Certified, with National Boards, wishes group or associate type practice in Connecticut. Presently in practice with Connecticut license. Military obligation completed.

PREVENTIVE MEDICINE—35 years of age, wishes institutional or industrial type practice in Connecticut. Presently in practice with Connecticut license. Available immediately.

INTERNIST—32 years of age, Eligible with National Boards, wishes solo type practice in Connecticut. Presently in practice with Connecticut license.

ANESTHESIOLOGY—38 years of age, Certified, wishes group or associate type practice in Connecticut. Presently in practice with Connecticut license. Military obligation completed. Available immediately.

SURGEON—35 years of age, Certified, wishes group, associate or institutional type practice in Connecticut. Presently in practice with Connecticut license. Military obligation completed. Available immediately.

PEDIATRICS—31 years of age, Eligible with National Boards, wishes group type practice in Connecticut. Group practice at large teaching hospital or university hospital preferred.

GENERAL PRACTICE OR PEDIATRICS—32 years of age wishes part-time position for the month of July.

INTERNIST—31 years of age, Eligible with National Boards, wishes solo, group or associate type practice in Connecticut. Interested in the area along the southern coast of Connecticut between 40 and 120 miles from New York City.

PHYSICAL MEDICINE AND REHABILITATION-ELECTRO NEUROMYOGRAPHY DIAGNOSIS—44 years of age, Board eligible, wishes group, associate or full time institution practice. Available mid-summer.

ANATOMIC PATHOLOGY—38 years of age, Certified, wishes to practice in Connecticut. Military obligation completed. Available immediately.

ANESTHESIOLOGY—56 years of age, Certified, wishes group, associate, institutional or industrial type practice in Connecticut. Available immediately.

PHYSICIAN-COLLEGE HEALTH — 26 years of age, with National Boards, wishes group or associate type practice in Connecticut.

OB & GYN—37 years of age, Certified, wishes associate or group type practice in Connecticut. Presently in practice with Connecticut license.

PHYSICIAN—26 years of age, wishes group type practice in Connecticut. Available mid-summer.

INTERNIST—32 years of age, Eligible with National Boards, wishes group or associate type practice in Connecticut. Seeking a position in internal medicine with an emphasis on chest disease preferably associated with a hospital where he can provide pulmonary function testing and good respiratory care.

ANATOMIC & CLINICAL PATHOLOGY — 34 years of age, Eligible with National Boards, wishes solo or associate type practice in Connecticut. Military obligation completed.

SURGEON—32 years of age, Eligible with National Boards, wishes solo, group or associate type practice in Connecticut.

INTERNAL MEDICINE-GASTROENTEROLOGY—31 years of age, Eligible with National Boards, wishes group or associate type practice in Connecticut.

PEDIATRICIAN—30 years of age, Board Eligible with Connecticut license. Desires associate type practice in Connecticut leading to partnership with another pediatrician or group practice.

INTERNIST—38 years of age, Certified with National Boards, wishes solo or associate type practice in Connecticut. Presently in practice. Military obligation completed. Available immediately.

ANESTHESIOLOGIST—36 years of age, Certified, wishes group, associate or institutional type practice in Connecticut. Seeking position where he could use his experience in respiratory care and anesthesia for cardio-pulmonary surgery. Presently in practice.

UROLOGIST—34 years of age, Certified, wishes group or associate type practice in Connecticut. Presently in practice.

OBSTETRICS AND GYNECOLOGY—35 years of age, Eligible with Connecticut license, wishes group, associate or institutional type practice in Connecticut.

OPHTHALMOLOGIST—49 years of age, Certified, wishes solo type practice in Connecticut. Presently in practice, Military obligation completed.

INTERNIST—31 years of age, Certified with National Boards, wishes solo or group type practice in

Connecticut. Presently in practice. With Connecticut license.

PEDIATRIAN—39 years of age, Certified with Connecticut license, wishes institutional type practice in Connecticut. Available now.

OPHTHALMALOGIST—39 years of age, Certified with National Boards, wishes solo or associate type practice in Connecticut. Presently in practice. Military obligation completed. Available anytime.

INTERNIST—34 years of age, Eligible, wishes to practice in Connecticut. Military obligation completed.

PATHOLOGIST—38 years of age, Certified, wishes group type practice in Connecticut.

SURGEON—33 years of age, Certified with National Boards, wishes group or associate type practice in Connecticut. Presently in practice. Available immediately.

ANYONE INTERESTED IN THE ABOVE IS ASKED TO CONTACT THE PHYSICIANS PLACEMENT SERVICE, 160 ST. RONAN STREET, NEW HAVEN, CONNECTICUT 06511.

Placement Opportunities

PEDIATRICIAN needed for multispecialty group in central Connecticut. Excellent starting salary; bonus arrangement, partnership after two years. Contact R. Postl, Business Manager, Grove Hill Clinic, New Britain, 203-225-8471.

GENERALIST wanted to take over lucrative practice in southeastern Connecticut village. Excellent opportunity for semi-retired physician. Box 95, Old Lyme, Connecticut 06371.

NEW MILFORD, CONN. community hospital of 79 beds, with an ICCU and planned expansion to 150 beds. Located on Candlewood Lake, one hour from Long Island Sound, and one and one half hours from New York City. We have a rapid population growth rate, excellent schools, and skilled-level industry. Further details are available from Dr. Randall Hays, M.D., Chief of Staff, New Milford Hospital, New Milford, Connecticut 06776.

PHYSICIANS needed in the following general specialties: Allergy, Anesthesiology, Dermatology, Internal and General Medicine, Psychiatry, Gastroenterology, and Otorhinolaryngology to practice in Torrington, Connecticut and surrounding communities. Modern 191 bed general, short term, voluntary, hospital, with all major medical and surgical specialties represented, serves a population of 50,000. Need to augment the Medical Staff due to immediate past and future retirement of active members of the Medical Staff as well as anticipated population increase during the next 10 years. Hospital is located in the center of Litchfield County, one of the most scenic parts of New England. Area offers excellent recreational facilities and is one hour from New Haven and Hartford, two hours from New York, and three hours from Boston. Search Committee of the Medical Staff will assist qualified candidates. Write or call: Thomas H. Walker, M.D., Chairman of Search Committee, The Charlotte Hungerford Hospital, Torrington, Connecticut 06790. Phone: (203) 489-0441.

MEDICAL OFFICE, its furniture and patient's records of internist leaving his practice for full time job, will be available at the end of June 1970 in Stratford, Connecticut.

PEDIATRICIAN—Partner leaving July 1st and need help in busy pediatric practice. Excellent salary leading to full partnership. Contact Charles Woods, M.D., 400 Stillson Road, Fairfield, Connecticut 06430.

CONNECTICUT-PSYCHIATRIC RESIDENCIES Geographically decentralized 1500-bed hospital. Approved 3-year program providing intensive training and experience with individual supervision in all psychiatric modalities. Visiting lecturers. Seminars. Associated with Yale University Department of Phychiatry and Neurology. All senior administrators and training director Board certified and on the faculty of Yale University. Stipends: First year, $10,694; Second year, $11,289; Third year, $13,020. Liberal benefits, including free hospitalization. Please send all particulars with first letter to Mehadin K. Arafeh, M.D., Supt. Connecticut Valley Hospital, Box 351, Middletown, Connecticut 06457.

CONNECTICUT-SENIOR PSYCHIATRISTS—in a 3-year accredited dynamic, decentralized community-oriented mental hospital. Affiliated with Yale University, Wesleyan University, and University of Connecticut. Excellent opportunities for professional growth and advancement. Salary commensurate with experience and training. Psychiatrist I, $19,303; Psychiatrist II, $20,128; Psychiatrist III, $21,911. Liberal benefits. Eligibility for Connecticut license required. Send all particulars in first letter, including references, to Mehadin K. Arafeh, M.D., Superintendent, Connecticut Valley Hospital, Box 351, Middletown, Connecticut 06457.

EMERGENCY ROOM—Full-time preferred in 250 bed Bristol Hospital. General Practitioner or specialist. To join 3 full-time plus part-time physicians rendering 24 hour medical coverage to 55,000 community. Excellent, new facilities, nursing and specialty backup. Salary plus liberal benefits for full-time. Call or write Richard P. Fredericks, Administrator, Bristol Hospital, Brewster Road, Bristol, Connecticut 06010. Telephone 589-2000.

IDEAL OPPORTUNITY—for any professional desirable of choice location for offices. Main Street, first floor. Three separate rooms completely air conditioned. Panelling throughout, one room installed with wall-to-wall rug. Two individual wash rooms. Ample free parking. Sufficient lighting, heat, and hot water.

VACANCY FOR A PART-TIME PHYSICIAN—to serve as District Medical Consultant in Putnam. Duties involve essentially reviewing medical report, ascertaining disabilities, and advising vocational counselors in related medical matters. Connecticut license required. One hour per week. Job would be particularly interesting to physicians who are phasing out current private practice. For further information, please contact Mr. Clay White, District Supervisor, Connecticut State Division of Vocational Rehabilitation, Norwich District Office, 257 Main Street, Norwich. Telephone 887-3546.

The Connecticut State Medical Society offers placement assistance through the Physician Placement Service, 160 St. Ronan Street, New Haven, Connecticut, 06511. This service is for the use of physicians seeking locations, as well as physicians seeking associates, and is without charge.

ANYONE INTERESTED IN THE ABOVE IS ASKED TO CONTACT THE EXECUTIVE DIRECTOR'S OFFICE, 160 ST. RONAN STREET, NEW HAVEN, CONNECTICUT 06511.

Members of the Connecticut State Medical Society reading papers before other organizations are requested to submit their papers to the JOURNAL for consideration by the Board of Editors for publication. Please send them to:

Louis H. Nahum, M.D., *Editor*
CONNECTICUT MEDICINE
160 St. Ronan Street
New Haven, Connecticut 06511

Welcome, New Members

New Haven County

William H. Baird, M. D., Gaylord Hospital, Wallingford, Conn. 06492.

Earl L. Baker, M.D., 314 Elizabeth Street, Derby, Conn. 06418.

Andre R. Boissevain, M.D., 31 Elm Street, Seymour, Conn. 06483.

Remo Fabbri, Jr., M.D., Yale New Haven Hospital, New Haven, Conn. 06504

Chester S. Kucinski, M.D., 333 Cedar Street, New Haven, Conn. 06510.

Jose D. Llibre, M.D., 310 Cedar Street, New Haven, Conn. 06510.

Robert F. McGann, M.D., 244 Main Street, South Meriden, Conn. 06450.

David F. Musto, M.D., 333 Cedar Street, New Haven, Conn. 06510.

Daniel S. P. Schubert, M.D., V.A. Hospital, West Haven, Conn. 06516.

Frank A. Sparrow, M.D., The Choate School, Wallingford, Conn. 06492.

Marc J. Taylor, M.D., V.A. Hospital, West Haven, Conn. 06516.

Joseph A. Vincitorio, M.D., 163 Grove Street, Waterbury, Conn. 06710.

Donald J. Weber, M.D., St. Mary's Hospital, Waterbury, Conn. 06720.

Fairfield County

Sumner G. Berkun, M.D., 881 Lafayette Street, Bridgeport, Conn. 06603.

Donald T. Evans, M.D., 43 South Main Street, Newtown, Conn. 06470.

Gerald Grossman, M.D., 1200 Summer Street, Stamford, Conn. 06905.

Isaac Horowitz, M.D., 881 Lafayette Street, Bridgeport, Conn. 06603.

George Kraus, M.D., Dept of Health, Greenwich, Conn. 06830.

Edward Littman, M.D., 83 East Avenue, Norwalk, Conn. 06851.

Francis W. Mergenthaler, M.D., 2660 Main Street, Bridgeport, Conn. 06606.

Arthur S. Mode, M.D., 21 Beachview Drive, Stamford, Conn. 06902.

Arthur P. Mostel, M.D., 27 Strawberry Hill Avenue, Stamford, Conn. 06902.

John A. Nagle, M.D., 23 Hoyt Street, Stamford, Conn. 06905.

Harry D. Orr, M.D., Hall-Brooke Hospital, Westport, Conn. 06880.

Sedat Ozcomert, M.D., 110 Glenbrook Road, Stamford, Conn. 06902.

Marvin L. Prince, M.D., 5 West Lane, Ridgefield, Conn. 06877.

James D. Prokop, M.D., 65 Prospect Street, Stamford, Conn. 06905.

Melvyn Rapoport, M.D., 50 Ridgefield Avenue, Bridgeport, Conn. 06610.

Nathaniel Selleck, M.D., 30 Hospital Avenue, Danbury, Conn. 06810.

John A. Semmelmeyer, M.D., 125 Kings Highway North, Westport, Conn. 06880.

Warren T. Sherman, M.D., 92 Locust Avenue, Danbury, Conn. 06810.

Alan E. Zimmer, M.D., 95 Locust Avenue, Danbury, Conn. 06810.

Litchfield County

Joseph R. J. Curi, M.D., Pediatrics-Adolescent Medicine, Litchfield Hills Medical Center, Torrington, Conn. 06790.

Edward J. Montoni, M.D., Litchfield County Hospital, 115 Spencer Street, Winsted, Conn. 06098.

David B. Swift, M.D., P.O. Box 153, Lakeville, Conn. 06039.

Tolland County

Charles G. O'Connell, M.D., 57 Union Street, Rockville, Conn. 06066.

Windham County

Raymond K. Bopp, M.D., 150 Mansfield Avenue, Willimantic, Conn. 06226.

John J. Kriz, M.D., Day Kimball Hospital, Putnam, Conn. 06260.

Gerard J. Lawrence, M.D., 150 Mansfield Avenue, Willimantic, Conn. 06226.

Lucille K. Loeser, M.D., 132 Mansfield Avenue, Willimantic, Conn. 06226.

Gertrude L. Rucker, M.D., R.R. #1, Box 172A, Storrs, Conn. 06268.

Hartford County

Vernon G. Allport, M.D., 99 Pratt Street, Hartford, Conn. 06103.

Stewart Atkinson, M.D., 240 Ashley Street, Hartford, Conn. 06105.

Frederick J. Bachl, M.D., 1 Mill Lane, Farmington, Conn. 06032.

Metin Bedizel, M.D., Grove Hill Clinic, New Britain, Conn. 06050.

Carl H. Braren, M.D., Great Meadow Towers, 1800 Silas Deane Highway, Rocky Hill, Conn. 06067.

Louis Brown, M.D., 33 Ledyard Avenue, Bloomfield, Conn. 06002.

Rudolfo G. Bulaong, M.D., 100 Constitution Plaza, Hartford, Conn. 06103.

John G. Freymann, M.D., 80 Seymour Street, Hartford, Conn. 06115.

William J. Geary, M.D., 350 Farmington Avenue, Hartford, Conn. 06105.

David J. Gorman, M.D., 51 Gillett Street, Hartford, Conn. 06105.

Hossain Hendessi, M.D., 320 Main Street, Manchester, Conn. 06040.

Samuel C. Himelstein, M.D., 810 Enfield Street, Enfield, Conn. 06030.

Mark A. Immergut, M.D., 140 Woodland Street, Hartford, Conn. 06105.

Richard F. Jones, III, M.D., 85 Jefferson Street, Hartford, Conn. 06103.

Marvin S. Koff M.D., 200 Retreat Avenue, Hartford, Conn. 06103.

(Continued on Page 433)

SUMMARY OF PROCEEDINGS
HOUSE OF DELEGATES — ANNUAL MEETING
Hartford, Connecticut — May 12, 1970

Reports and Addresses

The House received reports and/or addresses from the President, the Secretary, the Treasurer, the Council, the President of the Woman's Auxiliary and a number of delegates from other state medical societies. The report of the Secretary and the address of the President are published at the end of this summary.

Elections

A full slate of officers, committees, representatives and advisors was elected for the terms prescribed by the Bylaws.

The officers elected are:

President: Morris A. Granoff, New Haven
President-Elect: Frederick C. Weber, Jr., Greenwich
Vice-President: David A. Grendon, Sharon
Secretary: Reginald C. Edson, West Hartford
Treasurer: Bernard A. Burnham, Waterbury
Speaker of the House of Delegates: Kenneth F. Brandon, Hartford
Vice-Speaker: Frank K. Abbot, Waterbury

Two Delegates and two Alternates to the American Medical Association—for the term January 1, 1971 to December 31, 1972:

J. Alfred Fabro, Torrington (D)
E. Tremain Bradley, Norwalk (A)
Michael A. Dean, Bridgeport (D)
Sidney L. Cramer, Hartford (A)
Councilor-at-Large: Stevens J. Martin, Hartford

Presentations and Awards

1970 CSMS Press Award:

A press award, consisting of a plaque and a check for $150, was presented to Mr. David H. Rhinelander, medical science writer for the *Hartford Courant*, for excellence in medical news reporting and feature writing.

AMA-ERF Grants:

Furnished by the American Medical Association's Education and Research Foundation, unrestricted grants were made as follows:

To Yale University School of Medicine—$4,516
To UConn School of Medicine—$3,105

Since 1951, AMA-ERF has distributed such unrestricted grants in a total amount of over $21 million to some 85 approved medical school in the United States and Canada. The fund is supported by voluntary contributions from physicians and their families.

Presentation to Retiring President:

In appreciation of his untiring efforts on behalf of the Society and its members during 1969-70, Stevens J. Martin, Hartford, received an engraved silver bowl and a Past President's Pin as he completed his term of office. The presentation was made by Norman H. Gardner, East Hampton, Immediate Past President.

Presentation to Incoming President:

At the Annual Dinner on May 13, 1970, an engraved gavel, symbolic of his office, was received by Morris A. Granoff, New Haven, incoming President. The presentation was made by Stevens J. Martin, Hartford, retiring President.

Principal Actions Taken

Continuing the procedure established several years ago, all business coming before the House was referred to, and heard by, Reference Committees. Then, receiving the reports of the Reference Committees, the Delegates took actions as follows:

Reference Committee "A"

(1) *Address of the President:* Voted to accept "with an expression of sincere gratitude to Dr. Stevens J. Martin for an exemplary report".

(2) *Address of President of CSMS Woman's Auxiliary:* Voted to accept the address of Mrs. James F. Jones, Danielson, with commendation; emphasized the need for more physicians' wives to participate in the functions of the Auxiliary; and noted the commendable efforts being made to involve the wives of medical students, interns and residents in Auxiliary activities.

(3) *Liaison Committee with Welfare Department:* Approved recommendation that "the House of Delegates request the component County Medical Associations to submit to the Council forthwith the name of five or more members to be considered by the Council for appointment to a new "Medical Advisory Committee" for the Medicaid Program, such Committee to be made up of representatives of all or most types of general and special practice.

(4) *Patients' Free Choice of Physician and Hospital:* Voted to adopt a substitute resolution on this subject, instead of the one introduced originally by the New Haven County Medical Association. The "resolves" follow:

RESOLVED: That the House of Delegates of CSMS endorse the concept that all patients receive health care services by a physician of their choice at a hospital of their choice, within the framework of the competence of the physician to provide such services at the facility chosen; and be it further

RESOLVED: That the House of Delegates approve the concept of an "open hospital staff", in accordance with the subject policies of CSMS, the AMA and the Joint Commission on Accreditation of Hospitals, and refer this matter to the CSMS Committee on Hospitals for study, implementation and report to the House of Delegates at its next meeting.

Reference Committee "B"

(1) *Funding Health Manpower Training:* Voted to urge the AMA to take lead in endorsing Federal assistance to those agencies and industries responsible for the manpower and knowledge on which the distribution and quality of medical care will continue to depend.

(2) *Lead Poisoning:* Voted to advise the CSMS Committee on Public Health of the House's widening concern over lead poisoning as a health problem, and request the Committee to study and make recommendations to the Council regarding ways and means of alerting physicians and the public to the dangers of lead poisoning.

(3) *Health Careers Activities:* Voted to urge the Committee's reactivation, including the development and publishing of updated pamphlets or brochures for distribution to schools and colleges in Connecticut, the seeking of greater and more regular assistance from members of the Woman's Auixiliaries (state and county), and planning programs to increase health career recruitment for submission to the Council for approval and funding.

(4) *Physicians as Members of Hospital Governing Bodies:* Voted to adopt a subject resolution as follows:

RESOLVED: That the House of Delegates of CSMS endorse the position that physicians shall be eligible for, and should be included on, the membership of hospital governing bodies in the same manner that are all knowledgeable and effective individuals, and that such representation be strongly urged and submitted to the administrator and president of the board of trustees of all hospitals in Connecticut; and be it further

RESOLVED: That the House of Delegates make note of the fact that the Joint Commission on Accreditation of Hospitals has progressively supported this position, and, further, supports the position that individual members of the medical staff be considered for appointment as members of governing body committees.

(5) *Connecticut Regional Medical Program:* Voted to urge CRMP to cooperate more closely with the Council and the CSMS Committee on Postgraduate Education in the planning and implementation of continuing education programs for practicing physicians; also voted to check closely with CRMP as to what steps are being taken to preserve the confidentiality of patients' records under the CUPISS Program and to advise the medical staffs of Connecticut hospitals to be convinced that such confidentiality is being preserved before approving hospital participation in CUPISS.

(6) *Definition of Death:* Voted to approve a subject definition as follows: "In patients whose cardiorespiratory system is being supported by artificial means, death may be determined on the basis of complete and irreversible loss of function of the entire brain, from an evident cause, as established by current and recognized scientific and clinical methods. In case of (contemplated) organ or tissue transplantation, death of the donor must be established by at least two physicians who are not involved in such transplantation to the donee.

Reference Committee "C"

(1) *CSMS Position on Abortion Law Reform:* Voted to await a definitive report from the Ad Hoc Committee to Study Abortion to the Council before deciding what features of abortion law reform the Society should support and/or sponsor as a bill at the 1971 General Assembly.

(2) *Meetings of the House of Delegates:* Agreed with the contention of the Middlesex County Medical Association that, because of the ever-increasing amount of business to be acted upon by the House of Delegates, the House should meet more frequently or for longer periods or both. Voted to approve a recommendation of the Reference Committee that the semi-annual

meeting of the House of Delegates be increased from a one-half day to a full-day session, complete with reference committee hearings; that the format for annual meetings of the House be given further study by the Council, in the light of this year's experience and that of recent years; and that the calling of additional meetings (beside semi-annual and annual) be left to the discretion of the Council and the Staff, depending on the amount and urgency of business needing to be brought before the House.

(3) *Activities of the AMA:* It was voted *not* to adopt a resolution which advocated that the American Medical Association terminate its activities in the socio-economic field and devote all its energies to the areas of science and medical education.

(4) *Yale Medical Students' Action:* A resolution introduced on behalf of the students of the Yale University School of Medicine called for approval by the House of Delegates of a ten-day "strike" (absent-from-class) action voted by the medical student body and House endorsement of two objectives that the students decided to pursue; i.e., an end to "attempts to suppress legitimate dissent" and an immediate end "to escalation of the Vietnam war" and termination of "United States involvement there". After hearing extended testimony on this resolution from both Yale and UConn medical students, as well as from many members of the House, the Reference Committee recommended adoption of a substitute resolution which, with minor amendment, was adopted as follows:

RESOLVED: That the House of Delegates of CSMS commend the students at the Yale University and UConn Medical Schools for their determination to work constructively for the common good of the United States and all its citizens; and be it further

RESOLVED: That the House of Delegates deplore *not only* actions which seek to suppress legitimate dissent *but also* actions of dissent advocating the perpetration of violence to persons and institutions, those depriving others of the right to speak and be heard, those misusing our constitutional guarantees of freedoms so as to create civil disorder and cause senseless destruction of public and private property, the maiming of bodies and loss of life; and be it further

RESOLVED: That the House of Delegates encourage all members of the Society to communicate their views on foreign and domestic issues to their duly elected representatives.

Reference Committee "D"

(1) *Drug Abuse Educational Programs:* Voted to adopt a substitute subject resolution, recommended by the Reference Committee, as follows:

RESOLVED: That the House of Delegates, through the Council, initiate for the membership and the public-at-large an educational program covering all aspects of drug abuse; and be it further

RESOLVED: That the House of Delegates instruct the Council to appoint a committee of drug educators, intensively trained in the principles of drug research and the prevention of drug abuse, to carry out such educational program.

(2) *Alcoholism and Drug Dependency Among Physicians:* Voted to request the AMA to issue guidelines regarding methods to deal with mental disorders, alcoholism and drug dependency among physicians in order to provide all safeguards for both patients (the public) and the physician.

(3) *Civilian Practice as Alternative to Military Service:* Voted to approve a recommendation of the Reference Committee that a subject resolution *not* be adopted. The Committee's recommendation was based on the testimony of several medical students that they would not wish to be given "special privilege" and that such an option would only serve "as an escape mechanism to avoid military service" and would not result in high quality care being made available in the rural or disadvantaged area to which they were assigned. The recommendation was also based on testimony of CSMS members that the alternative proposed would "invite government invasion of civilian practice" and would constitute "a social, rather than a medical, program".

(4) *"Control of Dangerous Substances (Drugs) Legislation:* Voted to approve the Reference Committee's recommendation that the Society support the "Hughes Bill", S.3562, which would retain control of dangerous substances (including drugs) in the Department of Health, Education and Welfare, and not transfer control to the Department of Justice (as Senator Dodd's bill—S.3246—proposes).

ADDRESS OF THE PRESIDENT

Stevens J. Martin, Hartford

The Greek philosopher, Heraclitus, once observed that "life is in a continual state of flux". Since the days of Heraclitus, biologists have proven that his observation was true and have further demonstrated that flux—and the changes that it engenders—can be detrimental and regressive, or, if channeled in the right direction, can bring about progress in an orderly and constructive way. In many ways, the practice of medicine is like life itself—being in a constant state of flux and subjected to endless internal and external pressures for change. Hence, our ability to differentiate between change for progress and change-for-change's-sake will unquestionably determine the future course of our chosen profession.

One of the most important functions of an organization such as our State Medical Society is to try to keep abreast of as many as possible of the thousand-and-one proposals to revise or remodel the American system of medical care—proposals which differ in concept and approach, one from another, to as great an extent as does a single suture to repair a minor laceration from the most major of major operations. While I do not advocate rigid maintenance of the *status quo* in medical practice, it is my belief that the Society has an obligation—until directed otherwise by the membership—to attempt to preserve what is best in our present system while, at the same time, a responsibility to influence the nature and application of such changes as are desirable or are made inevitable through legislation. Under no circumstances can we afford to be apathetic; neither can we afford to be too inflexible nor—as some advocate—too radical. History has demonstrated that, in the evolution of all sciences, a constant and strong effort to provide prudent guidance to the evolutionary process has, more often than not, resulted in the salvation and nourishment of life—whether the life be that of a cell, a thought or the practice of medicine.

As I take stock of the events which have transpired in the Connecticut medical community in the past year, from my vantage point as your president, I believe I can say that some of these have been beneficial and have merited our support; that some of them have been ill-conceived and have merited our opposition; and that a few—such as the General Assembly's decision to dismantle a model Medicaid program—have resulted in frustration and disappointment, not only for the profession but also for the public we serve.

Cost control of hospital care services is a matter of paramount concern and we have tried to move constructively in this important area. The resolution this House of Delegates sent on to the AMA last December was, after minor amendment, returned to us as a workable policy statement which advocates that medical staffs and hospital administrations make cooperative efforts to keep the costs of hospital care services at the lowest levels consistent with the maintenance of high quality. Such efforts will certainly entail plans to increase the use of outpatient and ambulatory services, both diagnostic and therapeutic; the limitation of emergency room services to real emergencies; greater selectivity, based on real indication, in the number and variety of laboratory tests ordered; the avoidance of duplication of expensive equipment and services among hospitals serving the same area; and the distribution of the costs of hospital education programs among all residents of the community, rather than only among patients admitted to the hospital. It is hoped that these cooperative efforts will help to resolve the disturbing problem of ever-increasing hospital care costs.

The national shortage of physicians and all types of allied medical personnel is another problem which is in need of solution. Our Committee on Allied Medical Services, under the able chairmanship of Dr. Hilliard Spitz of New London, has devoted many hours of thoughtful study to this matter, and, with Council approval and encouragement, is initiating some first constructive steps toward helping to relieve the situation. In addition to reviewing several proposals to provide training for new types of health care technicians, and providing an advisory panel of Society members to assist the Commission for Higher Education in planning the curricula for technician training courses in community hospitals throughout the state, the Committee has arranged and will put on a Conference on the Changing Role in Nurse-Physician Relationship in the Delivery of Health Care Services. The Conference will be held in New Haven, at the Park Plaza Hotel, on May 27th, and is co-sponsored by the Connecticut Nurses Association, the Connecticut League for Nursing and the Connecticut Hospital Association. A large audience of physicians, nurses, technicians and hospital administration personnel is expected, and all who have participated in the planning for this important function deserve our heartfelt commendation.

With respect to the efforts being made nationwide to increase the number of physicians and already recognized paramedical personnel, as well as to create new types of technicians and assistants, I believe that a word of caution is in order. I think that it would be a serious, and perhaps disastrous, mistake to become so enthusiastic about increasing *the numbers* of health workers available to meet the needs of the American public that the all-important criterion of *quality* is somehow lost sight of. As physicians, we have an obligation to point out that errors of commission can be just as serious as errors of omission and to insist that paramedical personnel are not asked to assume, or have imposed upon them, responsibilities involving patient care which they are not really qualified to assume.

As I have mentioned previously, the medical practitioners of our State experienced a most frustrating development in 1969—namely the decision of the General Assembly to eliminate (by non-continuance) the usual and customary charge method for payment for physicians' services under the Medicaid Program. It is difficult for me to understand, as well as for many of the State legislators I have talked to during the past 5 months, the wisdom of drastically cutting the budget for Medicaid beneficiaries—and of instituting a fixed-fee policy of payment in place of the usual and customary method which proved so eminently successful in the first 10 months of its trial. It is no secret that, with the latter method, more patients were seen by more physicians (generalists and specialists) and yet the plan stayed within its budgetary limitations. With the new plan—the so-called fixed-fee plan or modification thereof—fewer patients are being seen privately and a significant decrease in the number of physicians participating has been noted. The plan may actually not be operating within its legal requirement that two-thirds of the practicing doctors be participants. But, permit me to cite the reaction of a physician who recently wrote to me—stating that "effective April 1, 1970, I will no longer be able to see State Welfare or ADC patients for routine check-ups or well-baby clinics." He sent a letter to his patients on Welfare or ADC with sincere regret stating:

"On March 1, 1969 the State Welfare Department significantly reduced fee payments to physicians in the State of Connecticut. Because of this as well as other problems associated with Welfare payments I have been seeing patients at a loss of money for the past year. I have done this because I feel a sincere obligation personally as well as on the part of the medical profession to provide medical care for all those who need it. On March 1, 1970 the Welfare Department reduced fee payments to medical specialists even further (by requiring pre-authorization forms etc.) and also eliminated all payments for immunizations and lab tests, etc. The net result of this was to force me to either practice poor medicine (i.e.: not perform indicated lab procedures, not give indicated immunizations, not be able to spend sufficient time with patients) or else suffer a prohibitive loss of money (i.e.: overhead, medical supplies, secretarial time, etc.)

After much consideration it became obvious that the only recourse open to me would be to stop seeing Welfare recipients for routine check-ups and well-baby visits. Any Welfare recipient who is in need of medical care because of illness *will be seen*. I must emphasize to you that sick patients will be seen without any remuneration. The patient will not be billed and no bill will be submitted to the Welfare Department."

I suspect that the decision which this one member feels he has been forced to make, however reluctantly, is the same decision that has been made by literally hundreds and hundreds of his privately practicing colleagues. We are hopeful that the final curtain has not yet fallen on the Medicaid Program. As I have already reported, for the Council, we are continuing our efforts to restore the best features of the dismantled program—not really for the benefit of the medical profession but for the benefit of the indigent and semi-indigent, many of whom experienced for the first time, during the trial year of 1968-69, the meaning of first-class medical citizenship.

As I look into the future—even without the aid of a crystal ball—I am cognizant of certain trends which have only recently made their appearance but which are bound to have effects on the practice of medicine as most of us have known it. Perhaps the most serious of these is the predicted "crisis" in American medical care that is anticipated to become most evident in the period 1975-80. The so-called crisis will be brought on—so say physicians, sociologists, economists and political pundits—not only by an increasing shortage of medical practitioners but also by an increasing problem of maldistribution of physicians in urban versus rural areas of the nation. Dr. Roger O. Egeberg, HEW Undersecretary for Medical Affairs, tells us that the nation's number one problem is the distribution of health care services. It is claimed by some that the current efforts of medical educators, physicians, the AMA, government, labor and the public-at-large may be too little and too late to prevent the impending crisis. I, for one, feel differently—a bit more optimistic—because I have confidence that the well-known American quality of "fighting hardest when hit" will enable us to meet this challenge successfully as we have done so often with others in the past. We have real problems to cope with—that no one can deny. But a crisis? I think not!

It appears most likely that a universal federal health insurance system is inevitable. I am certain, that if and when it arrives, it will be received with mixed blessings. Dr. Egberg feels that if it is enacted before 1977, "doctors will be completely swamped and you will have chaos." It is my fervent hope that a federal health insurance system will be developed—but not without the requested support of the AMA or perhaps even an AMA plan—and not without significant modification of our present Medicare and Medicaid programs.

Social questions and problems are becoming of increasing significance to all physicians, not the least of which is medicine. Doctor Howard H. Hiatt, of the Harvard Medical School, recently stated that it is the responsibility of *all* physicians, second only to (1) the care of the individual patient and (2) the necessity to nurture the scientific basis of medicine—"to become *involved in the consideration and resolution of social questions* that directly or indirectly affect the health of the nation or the world." He emphasized again our responsibility to society in providing adequate medical care, birth control, etc.

I would consider myself to be remiss in my duty as your president if I did not make mention of the recommendations and proposed implementation of the AMA Committee on Planning and Development (the Majority and Minority Report) which was presented at the Interim Session of the AMA last November and which was, in turn, submitted to us at state level for study and comment. Without question, this is the most far-reaching, constructive study conducted by the AMA in the last two decades. The recommendations concern problems of social, economic, legislative and legal aspects of the practice of medicine. Its final conclusion and acceptance will affect all of us. I hope you have taken the time to read the so-called "Himler" report carefully. I personally feel it is an outstanding study, and that the recommendations, with some revisions, are worthy of our support.

In conclusion, I wish to take this opportunity to express my sincere thanks to my fellow officers, to all members of this House, to countless committees and committee chairmen, and to our dedicated staff people, for the help they have given me during this past year of my service as president. Also, I express my heartfelt appreciation for the honor which has been mine in holding this high office, for the many rewarding experiences it has brought to me, and for the opportunity to make a contribution to the work of our Society and to the preservation of all that is good in the practice of medicine in Connecticut.

REPORT OF THE SECRETARY

Reginald C. Edson

Every physician has a share in the responsibility to see to it that the delivery of up-to-date medical service to the public becomes a reality.

There is much to be done—recruitment of potential health personnel, education for today and tomorrow for undergraduates and for postgraduates, preservation of the best of the old, adoption of the most promising of the new.

To preserve the health, heal and comfort the sick, sustain the dying and comfort the family—on a patient to physician clinical basis and leave the future of medical care to others, is not in the best interest of the patient.

The enumeration contained in this membership report is but a statistical exercise unless members convince non-members to assume the responsibility of membership, unless members participate in the preservation of the best of the old and the adoption of the best of the new. This requires careful choice of representative and self-commitment to personal service on a local, state and national basis.

Involvement is a prerequisite to progress. Your involvement is necessary.

MEMBERSHIP REPORT OF THE SECRETARY

FAIRFIELD COUNTY

Membership—January 1, 1969		1001
New Members	44	
Less:		
Deaths	14	
Resignations	13	
Tranfers	2	
Non-payment dues	10	
	39	
Net Gain		5
Membership—December 31, 1969		1006

HARTFORD COUNTY

Membership—January 1, 1969		1150
New Members	52	
Less:		
Deaths	19	
Resignations	13	
Transfers	3	
Non-payment dues	3	
	38	
Net Gain		14
Membership—December 31, 1969		1164

LITCHFIELD COUNTY

Membership—January 1, 1969		147
New Members	8	
Less:		
Deaths	1	
Resignations	0	
Transfers	1	
Non-payment dues	3	
	5	
Net Gain		3
Membership—December 31, 1969		150

MIDDLESEX COUNTY

Membership—January 1, 1969		120
New Members	11	
Less:		
Deaths	2	
Resignations	3	
Transfers	0	
Non-payment dues	1	
	6	
Net Gain		5
Membership—December 31, 1969		125

NEW HAVEN COUNTY

Membership—January 1, 1969		1029
New Members	53	
Less:		
Deaths	18	
Resignations	14	
Transfers	3	
Non-payment dues	5	
	40	
Net Gain		13
Membership—December 31, 1969		1042

NEW LONDON COUNTY

Membership—January 1, 1969		222
New Members	8	
Less:		
Deaths	9	
Resignations	1	
Transfers	2	
Non-payment dues	0	
	12	
Net Loss		4
Membership—December 31, 1969		218

TOLLAND COUNTY

Membership—January 1, 1969		29
New Members	4	
Less:		
Deaths	0	
Resignations	1	
Transfers	0	
Non-payment dues	0	
	1	
Net Gain		3
Membership—December 31, 1969		32

WINDHAM COUNTY

Membership—January 1, 1969		71
New Members	6	
Less:		
Deaths	0	
Resignations	1	
Transfers	1	
Non-payment dues	0	
	2	
Net Gain		4
Membership—December 31, 1969		75

ASSOCIATE MEMBERS	9
New Members	0
Less Deaths	1
Associate Members—December 31, 1969	8

TOTAL SOCIETY MEMBERSHIP—January 1, 1969		3769
New Members		186
		3955
Less:		
Deaths	63	
Resignations	46	
Transfers	12	
Non-payment dues	22	
		143
TOTAL SOCIETY MEMBERSHIP—December 31, 1969		3812
Net Gain for year		43

TOTALS

Fairfield	1006
Hartford	1164
Litchfield	150
Middlesex	125
New Haven	1042
New London	218
Tolland	32
Windham	75
	3812
Associate Members	8
	3820

(Continued from Page 425)

Edmund M. Lesko, M.D., 85 Jefferson Street, Hartford, Conn. 06103.

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AROUND THE STATE

New Haven County

Board of Governors New Haven County Medical Association

The New Haven County Medical Association's Board of Governors at its meeting of April 30, 1970 adopted the following partial list of legislative goals for 1970-1971:

1. *Abortion*—Abortions should be made a *responsible* matter of *Health* rather than *Law*.
2. *Health Education*—The last session's bill in the Connecticut legislature should be re-introduced.
3. *Title XIX*—The original Title 19 program should be re-introduced in the Connecticut legislature.
4. *Drug Control*—The current "Justice Department Controlled" Bill should be defeated in Congress.
5. *The AMA Bill*—The AMA bill for Voluntary National Health Insurance should be supported in Congress.

It could be noted that COMPAC, by any concept of logic, ought to be an aid that is viable and effective in these areas.

Today its effectiveness has been silenced by the Connecticut State Medical Society's own democratic vote in December 1969 rendered by the Connecticut State Medical Society House of Delegates.

Respectfully submitted,
William L. West, M.D., *Clerk*

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L-Dopa Therapy In Parkinson's Disease

(*Can. Med. Assoc. Jr.*: 101, 59, December 27, 1969, Barbeau, A.) The last 10 years have seen great activity in the investigation of cerebral catecholamines particular attention having been paid to dopamine. The low dopamine content in the basal ganglia and in the urine of patients with Parkinson's disease led to the logical use of the precursor DOPA in the treatment of this disorder.

Between 1961 and 1966 both the oral and the intravenous routes were utilized and some effects were noted upon akinesia and rigidity. The doses then used were low and the results remained somewhat controversial.

When higher oral levels of L-Dopa were introduced the beneficial action of L-Dopa upon Parkinsonian symptoms and signs proved beyond doubt, but there came to light a number of troublesome side effects, the worst of which were hypotension and a variety of abnormal involuntary movements.

Recently new approaches to the therapy have been tried and the sum total of these observations is to challenge our peace of mind regarding a seemingly logical chain of events. We are convinced that such second thoughts will eventually result in better and safer methods of treating this too frequent and disabling neurological disorder.—L.H.N.

Smoking Link Seen To Atherosclerosis

(*Geriatrics*, 25, 79, March 1970) Heavy smoking enhances the development of atherosclerosis, a Danish researcher has concluded after investigating smoking habits and carboxyhemoglobin and serum cholesterol levels in 1085 subjects.

Knud Kjeldsen found that smoking habits were different in 59 of the subjects in whom atherosclerotic cardiovascular disease was diagnosed than in the rest of the subjects; of those with the disease all but one were smokers and most of them were heavy smokers who inhaled. Furthermore, he found significantly higher levels of carboxyhemoglobin and serum cholesterol in these subjects.

The study also showed that healthy smokers had significantly higher serum cholesterol levels than non-smokers and that carboxyhemoglobin and cholesterol levels were significantly correlated.

The findings indicate that excessive smoking will lead to carboxyhemoglobin saturations of 8-19 per cent and that proper oxygenation of the vascular tissue will be impeded in these circumstances thereby enhancing atherogenesis.—L.H.N.

X-Ray of the Month

Section of Chest Diseases

Yale-New Haven Medical Center

Arnold B. Rilance, M.D., Director, Winchester Chest Clinics

History

J.B. #75-99-01. A 44 year old male metal worker, was admitted to the Yale-New Haven Hospital on 9/4/69, with the chief complaint of right-sided chest pain radiating to the neck. Starting twenty-four hours prior to admission, the patient, for the first time, noted pain in the anterolateral aspect of the right hemithorax. This was associated with malaise, fever and chills. The patient had no sputum. There was no history of previous respiratory illness. The patient was a moderately heavy smoker. There was no weakness or weight loss. There were no known allergies.

Physical Examination:

Blood pressure: 140/90; Pulse, 150; Temperature: 103.4; Respirations: 15.

Lungs:

Diminished breath sounds with egophony over the right anterior chest.

Laboratory Tests:

Tuberculin PPD, intermediate, – negative. WBC: 7,200. P-65. Sputum culture—pneumococci, Type III.

Treatment:

I. V. Penicillin

Diagnosis:

Pneumococcal pneumonia with bullous disease of the lungs.

Discussion

The rather bizarre appearance of this pneumonia consolidating around the hilum of the lung with

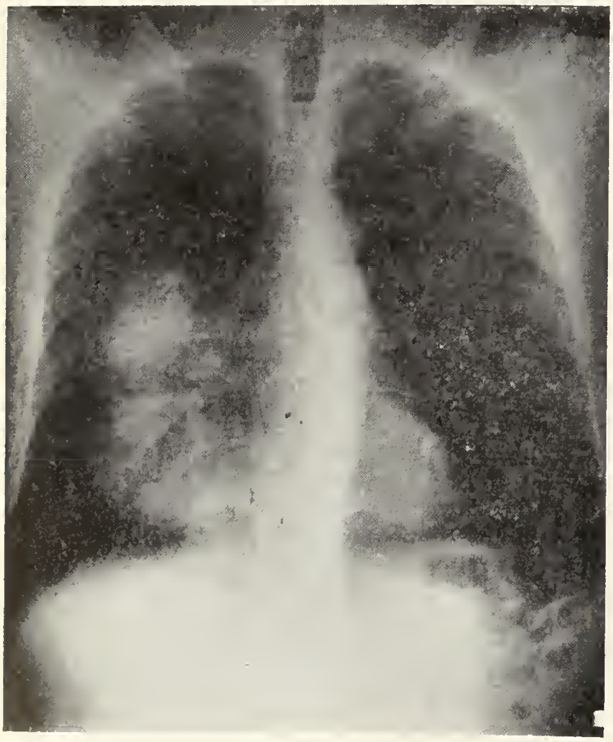

Figure 1

On admission. A large mass lesion confluent with the right hilum—sharply outlined—involving the anterior segment of the right upper lobe and right middle lobe. Note a well demonstrated air bronchogram ruling out neoplasm as the causative factor.

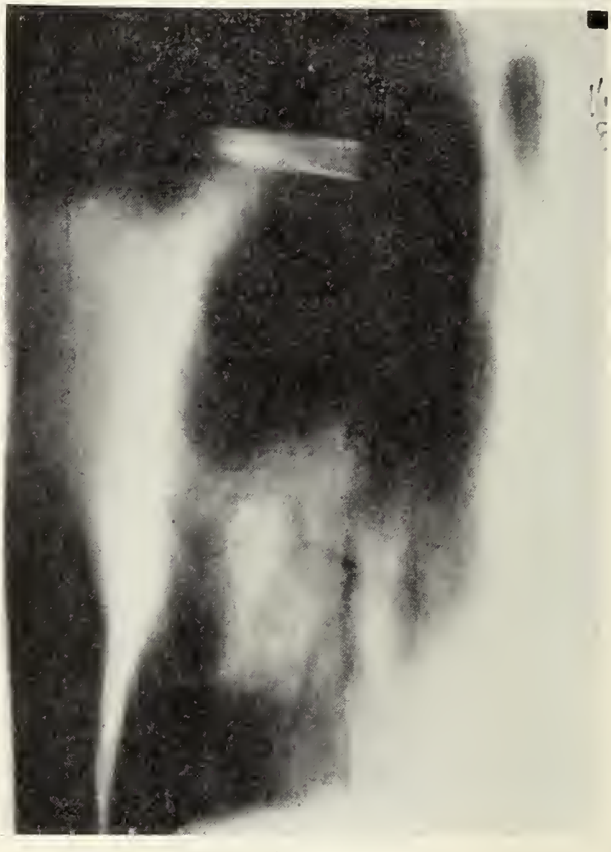

Figure 2

Laminographic cut to illustrate infiltration and bronchi in more detail.

peripheral segments of lung clear of infiltration is unusual. Superficially it simulates a tumor mass. Subsequent films demonstrate areas of large bullae formation in the peripheral segments of the lung distal to the pneumonia. It is postulated that these bullae were present prior to the development of the pneumonia and acted as a buffer to localize the pneumonia to the centrally located segments.

Noteworthy is the slow resolution of the pneumonia, very commonly found to occur in the presence of pulmonary emphysema or bullous disease.

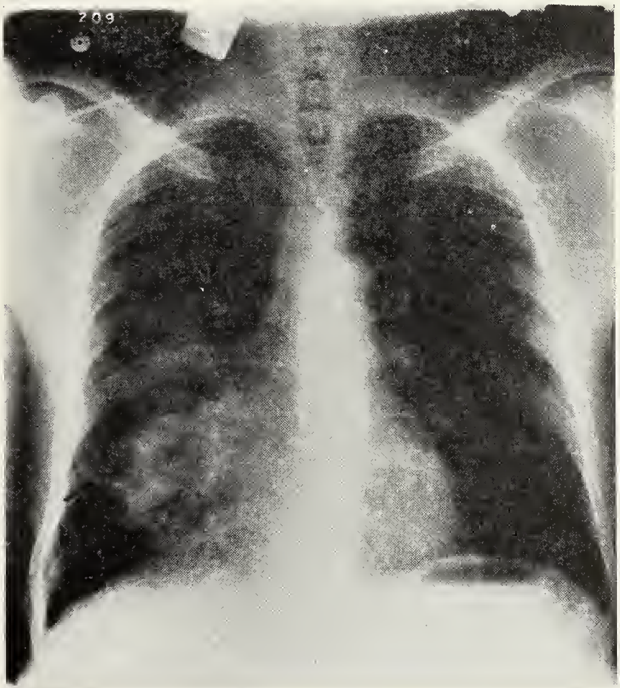

Figure 3
Illustrates slow resolution of pneumonia. The arrow points to a large bullous lesion at periphery of infiltration.

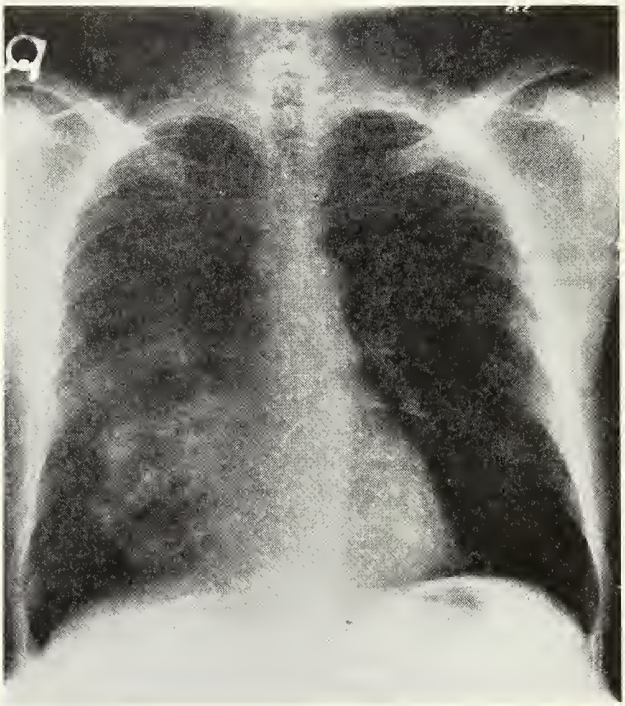

Figure 4
Further slow resolution, multiple poorly outlined bullae now seen.

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Electrocardiogram of the Month

Yale-New Haven Hospital
New Haven, Connecticut

Prepared by
HYMAN M. CHERNOFF, M.D.
Associate Professor of Clinical Medicine,
Yale School of Medicine
Director, Dept. of Electrocardiography
Memorial Unit, Yale-New Haven Hospital

Among the various factors which may influence the order and rate of the repolarization process in the ventricle is the level of ionizable calcium in the serum. Since the repolarization process is represented in the electrocardiogram by the ST segment and the T wave, certain specific changes in the contour and duration of the ST segment and T wave will occur in the presence of hypocalcemia and hypercalcemia. Careful study of the ST segment and T wave in the electrocardiogram of all patients may, therefore, lead to the discovery of an occult disorder of the parathyroid gland or to various other disorders of the body which are accompanied by alterations in serum calcium levels.

Experimental studies on the shape and duration of the transmembrane action potential in single ventricular fibers reveal that the repolarization process may be divided into two main phases. The first phase is slow and plateau-like and is followed by a second more rapid phase. The duration of the ST segment in the electrocardiogram corresponds approximately to the duration of the initial slow phase and the duration of the T wave to the duration of the second more rapid phase. The effects upon the repolarization process of a decrease or increase in the level of ionizable calcium is illustrated in Fig. 1.

Below are tracings obtained in several patients in whom abnormal calcium levels were first suspected from an inspection of the ST segment and T wave of routine electrocardiograms and by measurement of the K-QaT and K-QT values and later confirmed by laboratory determination of levels of ionizable calcium.

FIG. 1

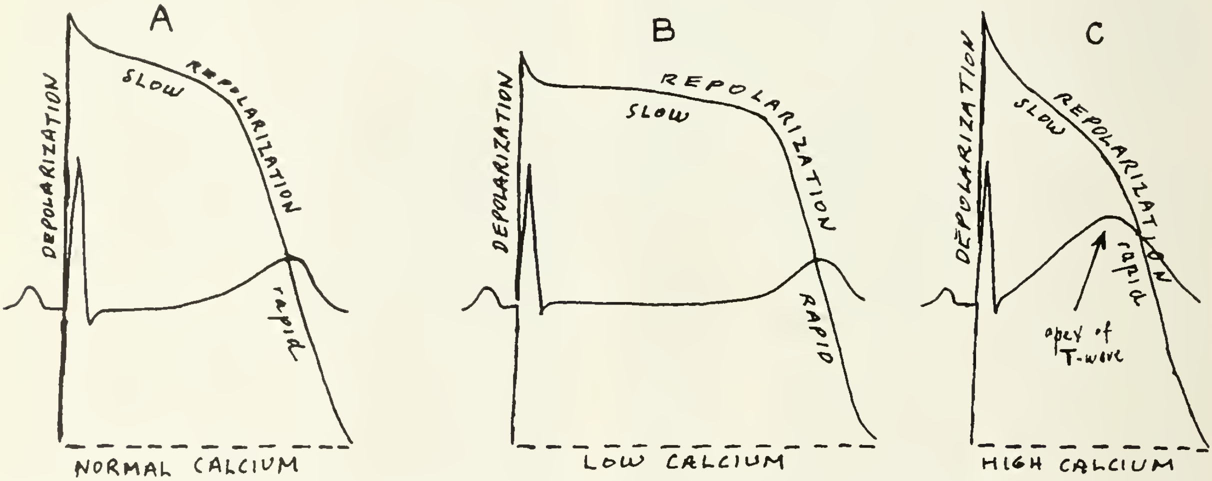

Diagram of action potential of single ventricular muscle fiber superimposed on the ECG. Note in *A*, when serum calcium levels are normal, that the initial slow phase of repolarization is of longer duration than the second rapid phase. In *B*, when the calcium level is low there is prolongation of the initial slow phase of repolarization and this is reflected in the ECG in a long isoelectric ST segment. As a consequence of this the QT interval is prolonged. In *C*, when the calcium level is high there is a more rapid initial phase of repolarization which is reflected in the ECG by shortening or virtual absence of the ST segment. As a consequence of this the QT interval is shortened. Since it is often difficult to measure the exact end of the T wave in order to obtain the QT value it has been found more useful to measure the interval between the onset of Q and the apex of the T wave (QaT). This interval is measured in whichever lead shows the largest monophasic wave. Since the duration of repolarization normally varies with heart rate, decreasing as the heart rate increases, the formula devised by Bazett may be used to obtain the K-QT and K-QaT values (where K-QT equals the observed QT interval divided by the square root of the R-R interval, and where K-QaT equals the observed QaT interval divided by the square root of the R-R interval). The normal values for K-QT have been found to range from 0.39 to 0.44 and the K-QaT value ranges between 0.28 and 0.32.

FIG. 2

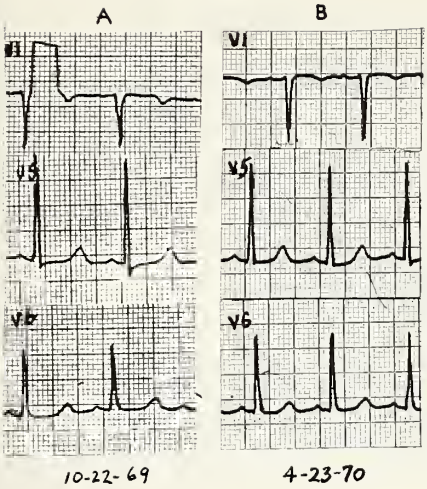

FIG. 3

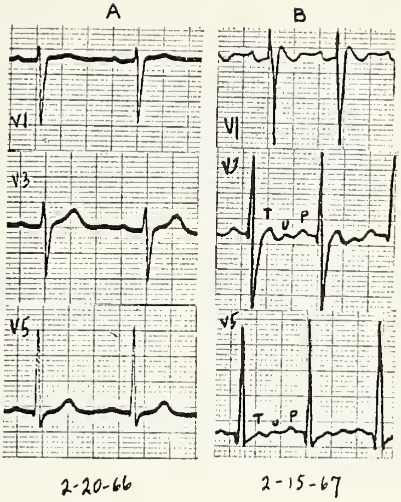

FIG. 4

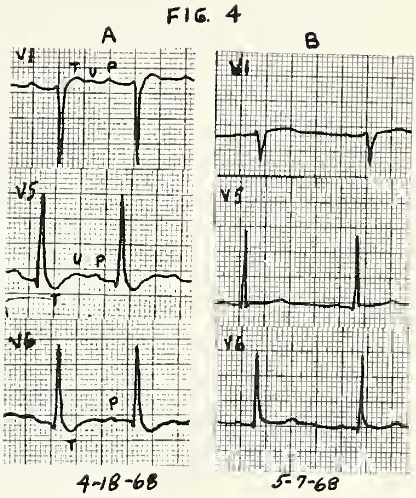

Figure 2

A—Routine ECG taken on 10-22-69 in 50 year old white female reveals a prolonged isoelectric ST segment. The QT interval measures 0.44 sec. The K-QT value is prolonged to 0.51. The serum calcium was found to be 6.2 mgm %. Clinical studies revealed the presence of hypo-parathyroidism.

B—Repeat ECG taken on 4-23-70 after 5 months of therapy with calcium and dihydrotachysterol. Note the decrease in length of the isoelectric ST segment. The QT interval measures 0.35 sec. The K-QT value is now within normal limits at 0.43.

Figure 3

A—Routine ECG taken on 2-20-66 in 55 year old white female with carcinoma of the breast. The QT interval measures 0.36 sec. The K-QT value is normal at 0.40.

B—Repeat tracing taken on 2-15-67 reveals virtual absence of the ST segment. The QT interval is 0.24 sec. The K-QT value is shortened to 0.32. The QaT interval measures 0.18 sec. The K-QaT value is shortened to 0.25, a level consistent with hypercalcemia. The serum calcium level was founl to be 15.0 mgm. %. X-ray studies revealed widespread bone metastases.

Figure 4

A—Routine ECG taken on 4-18-68 in 55 year old white female about to undergo repair of femoral hernia. There is virtual absence of the ST segment. The QT interval measures 0.22 sec. The K-QT value is shortened to 0.28. The QaT interval measures 0.15 sec. The K-QaT value is 0.20, consistent with hypercalcemia. The serum calcium level was found to be 17.0 mgm.%. Exploration of the neck revealed a small parathyroid adenoma.

B—Repeat tracing taken on 5-7-68 after removal of the parathyroid adenoma. The QT interval measures 0.38 sec. The K-QT value now is within normal limits at 0.40. The serum calcium level was found to be 9.5 mgm %.

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LAW—MEDICINE NOTES

J. Alfred Fabro, M.D.

The People, Plaintiff v. Belous, Defendant

In September 1969 the California Supreme Court in a 4-3 decision ruled that a California statute forbidding abortion except as necessary to preserve the life of the mother was unconstitutional on the ground of vagueness. This case is important and worth reviewing because it presents for the first time a major challenge on constitutional grounds to a state law which criminally punishes a physician for terminating pregnancy in its early stages.

The decision is particularly important because among state courts the California Supreme Court is outstanding and influential, and among the leaders when it comes to using the court to effect social change. Already a federal district court has followed its lead; and some proponents of liberalization of abortion laws are appealing to the courts after this decision.

Dr. Leon Phillip Belous was convicted January 1967, after a jury trial, of violating two sections of its Penal Code in regard to abortion, both felonies. He was fined $5,000 and placed on probation for two years. His scientific and professional credentials were of the highest. He was an American Board certified obstetrician and gynecologist, and on the Board of Directors of the California Committee on Therapeutic Abortion. He was on the attending staff of Cedars of Lebanon Hospital in Los Angeles.

The facts: A young pregnant woman and her fiancé, later husband, went to him for advice about an abortion. They had never heard of Dr. Belous until they heard him on television, advocating a change in the California abortion laws. He explained that he could do nothing, that he did not perform abortions. They threatened that they would go to Tijuana for an abortion, or get an abortion "one way or the other." He warned them about the dangers of criminal abortion. Finally he capitulated to their entreaties and gave them the name of an unlicensed doctor (Lairtus) in the area who did abortions and whose competence Dr. Belous could vouch for from personal observation. Lairtus was licensed in Mexico but not in California. Dr. Belous had seen him performing skilled and safe abortions in Mexico. She went to Lairtus' apartment and had the abortion.

While she was resting from the operation there, the police acting on a tip from someone else came and arrested Dr. Lairtus. They found notebooks there with other patients' and Dr. Belous' name. From this information they arrested him also.

The substance of Belous' defense was that he believed that the couple would, in fact, do anything to terminate pregnancy, which might involve "butchery" in Tijuana or self mutilation. He finally gave in and gave them the phone number of this competent though unlicensed doctor. He believed that unless he did so, her life would be endangered.

Organizations interested in civil liberties and legalized abortion submitted legal briefs supporting Dr. Belous. They argued that (1) the statute was an arbitrary invasion of the fundamental and constitutional right of a woman whether to bear offspring; (2) it was an arbitrary invasion of the right of a physician to prescribe for his patients in accordance with his best professional knowledge; (3) the state interest in prohibiting abortion by licensed physicians was not sufficiently compelling to be justified; (4) it violated the equal protection clause of the 14th amendment of the Federal Constitution because it discriminated against poor people who could not afford to get abortions under the present statute; (5) the statute was a reflection of particular religious views and thereby prohibited by the religious clause of the first amendment of the Federal Constitution.

The essence of the law was that any person who directly or indirectly participated in or procured an abortion except as "necessary to produce the miscarriage of any woman in order to save her life" shall be guilty of a felony.

The prosecution argued: "If medical science feels that the abortion should be performed as it is necessary to preserve her life, then it may be performed; that is, unless it is performed, the patient will die." Interested parties urged "that the state has a compelling interest in the protection of the embryo and

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DR. J. ALFRED FABRO, Senior Attending Surgical Staff of the Charlotte Hungerford Hospital, Torrington, Conn.

fetus and that such interest warrants the limitation on the woman's constitutional rights."

The court's decision: "We have concluded that the term 'necessary to preserve' . . . is not susceptible of a construction that does not violate legislative intent and that is sufficiently certain to satisfy due process requirements without improperly infringing on fundamental constitutional rights."

It is a well established principle of law that legislation have a reasonable degree of certainty, especially in criminal law. . . . "A statute which either forbids or requires the doing of an act in terms so vague that men of common intelligence must necessarily guess at its meaning and differ as to its application violates the first essential of due process of law.' '

The court held that neither dictionary definition nor judicial interpretations provided a clear unambiguous meaning for the word, "necessary" or "preserve," either individually or joined into the phrase, "necessary to preserve the life."

The court reminded the prosecution that California appellate courts, in reversing the conviction of physicians, had already rejected an interpretation of "necessary to preserve life" requiring certainty or immediacy of death. In one case, an obstetrician performed the abortion after receiving letters from two phychiatrists to the effect that abortion was indicated as necessary to save the woman's life from the "possibility" of suicide. The appelate court accepted this explanation.

In the other case the appellate court stated that the abortion statute "does not mean by the words, 'unless the same is necessary to preserve her life,' that the peril to life be imminent. It ought to be enough that the dangerous condition be potentially present, even though its full development might be delayed to a greater or lesser extent; nor was it essential that the doctor should believe that the death of the patient would be otherwise certain in order to justify him in affording present relief."

The court considered it significant that the Legislature, in amending the abortion statute in 1967, did not repudiate the legal rules set down by the courts in these two cases.

The Court also stated: "A definition requiring certainty of death would work an invalid abridgement of the woman's constitutional rights. The rights involved in the instant case are the woman's right to life and to choose whether to bear children. The woman's right to life is involved because childbirth involves risk of death.

"The fundamental right of the woman to choose whether to bear children follows from the U. S. Supreme Court's and this court's repeated acknowledgement of a 'right of privacy' or 'liberty' in matters related to marriage, family, and sex." Significantly the court added, "It is not surprising that none of the parties who had filed briefs in this case have disputed the existence of this fundamental right."

The court rejected the argument that the state has a compelling interest in the protection of the embryo and fetus, noting that all of the statutes and rules relied upon by the prosecution require a live birth or reflect the interest of the parents; and that the law treats the embryo, fetus, and born child differently.

"The intentional destruction of the born child is murder or manslaughter. The intentional destruction of the embryo or fetus is never treated as murder, and only rarely as manslaughter, but rather as the lesser offense of abortion." The legal rights of the fetus are conditioned on the fact that the baby be born alive.

Three judges dissented in two opinions. Two stated that if the doctor believed that the patient's life was in danger, he could have taken her to one of several hospitals in which therapeutic abortions were being performed. They stated that the words in the context were sufficiently clear, and that the issue of vagueness had never before been brought up.

One held that the mandate was plain and clear. He could not agree with the majority that the words or their meaning were not clear. These three would have upheld the conviction.

This 1969 decision invalidated the 1850 statute regarding an act done in 1966. In November 1967, California adopted a new Therapeutic Abortion Act. It would permit abortion during the first twenty weeks of pregnancy by a licensed physician in an accredited hospital if "there is substantial risk that continuance of the pregnancy would gravely impair the physical or mental health of the mother"; or that "the pregnancy resulted from rape or incest." Mental health includes mental illness to the extent that the woman would be dangerous to herself. The Governor signed the act only when a provision passed by the Legislature permitting abortion if there was a substantial risk that the baby might be born with serious mental or physical defect be deleted. It was.

The court was careful to state that it was not passing on the validity of this new Act. "Since the Act was adopted after the abortion in the instant case, we do not reach the issue of its validity."

The state has appealed the decision to the U. S. Supreme Court. Though the Belous decision has no binding effect on courts outside California, it already seems to have some effect. On November 10, 1969, for example, the federal district judge for the District of Columbia dismissed as unconstitutional because of vagueness a similar statute: "As necessary for the preservation of the woman's life or health. . . ."

The judge held that this phrase "fails to give that certainty which due process of law considers essential in a criminal statute. Its many ambiguities are particularly subject to criticism for the statute unquestionably impinges to an appreciable extent on significant constitutional rights of individuals.

"The jury's acceptance or non-acceptance of an individual doctor's interpretation of the ambivalent and uncertain word 'health' should not determine whether he stands convicted of a felony, facing ten years' imprisonment. His professional judgment made in good faith should not be challenged. There is no clear standard to guide either the doctor, the jury or the court. No body of medical knowledge delineates what degree of mental or physical health or combination of the two is required to make an abortion conducted by a competent physician legal or illegal under the code."

Nine states in the last two years have passed liberalized abortion laws. Bills have been, and will be, introduced in others.

The Belous decision means that all such statutes, including those liberalized, may be challenged on the ground of vagueness.

Even more significant in the opinion, however, was the court's dictum: "The rights involved in the instant case are the woman's rights to life and to choose whether to bear children."

Four New York parties have since challenged in a federal district court the constitutionality of its abortion law, similar to California's statute overruled in the Belous case, on the ground that a woman has the right to determine for herself whether or not to bear a child, a right guaranteed by the Federal Constitution.

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Letter To The Editor

Members of the Society are invited to communicate with the Editor expressing their opinions or giving information as to any matter of interest to the members. The Editorial Board reserves to itself the right to select the communications or excerpts therefrom that will be published and to reject others. As with other material which is submitted for publication, all letters will be subject to the usual editing. Address all correspondence to: THE EDITOR, CONNECTICUT MEDICINE, 160 St. Ronan Street, New Haven, Connecticut 06511.

To the Editor:

Hypertension or high blood pressure may be a manifestation of any of several disease processes. One of these, renal responsibility involves the patient in complex testing procedures. In a recent article which appeared in the J.A.M.A. of 1969, Vol. 47:145 under the heading, "Renal Artery and Hypertension, Observations on Current States of Therapy from a Study of 115 Patients." by Alvin Shapiro, M.D. et al. University of Pittsburgh Medical School, the author and his co-workers based a very comprehensive and detailed report on observations made over the period from 1962 through 1966 on a group of 115 patients.

Their special concern was Renal Artery Stenosis and resultant ischaemia. In arriving at decisions they made use of the various tests extant, including pyelograpry, aortography, split function tests via cystoscopy, angiotensin infusion, pressor and renin activity among others. They concluded the finding of renal ischemia or constrictions of the renal artery is not always the decisive factor in deciding on treatment. In older age groups, especially, surgical correction will not produce the same results as those obtained in younger adults. My demonstration of blood pressure improvement before surgery could be very helpful.

From articles appearing in journals and personal letters to your correspondent, one learns that renal artery sclerosis with attending restricted renal blood flow leads to ischemia of the organ. Such ischaemia may follow other processes which involve the kidney such as pyelonephritis and arterioscelerotic kidney disease, conditions which suggest widespread vascular obliteration rather uniformly throughout the medulla of both kidneys.

Leonhardt and Landes in the J.A.M.A. reported that there is a higher Puo$_2$ obtained from the urine of the ischemic than from the normal kidney. Normally, in the process of cell separation and by the countercurrent mechanism, urine approaches equilibration with that of the surrounding capillary blood. They write there is little doubt the Puo$_2$ of the glomerular filtrate equals that of the arterial blood from which it is derived. By accepting this statement a finding of a higher than normal Puo$_2$ in the urine of the kidney pelvis, one may read a higher than normal Po$_2$ in the capillaries surrounding the terminal renal tubules.

At this point I would like to call your attention to my original observation involving the use of indigocarmine in a study of hypertensives in which systolic and diastolic pressure were lowered remarkably in relation to the time of the appearance of the dye in the urine, the intensity of the dye elimination and the length or duration of its excretion. This does not happen in every trial case. It is significant since a) a full intense output of the dye may not be accompanied by any drop in pressure or b) in some instances blood pressure will rise and c) since no or scant elimination has allowed the dye to act on receptors and/or volume regulatory areas elsewhere in the body without a pressure change, so a direct attack on some special change in the kidney by the dye must be accepted. This experience has repeated itself numerous times, under various conditions and readings by different individuals.

In a communication such as this one cannot dilate on probable causes. The theory, if such it is, of renal ischemia with increased Po$_2$ responsibility for a blood vessel spasm or contracture is very intriguing. In Connecticut Medicine, Vol. 31, No. 1, Jan. '67 the Editor, L.H.N. cited Carmody and Clark: "O$_2$ is the physiological stimulus for contraction and closure of the ductus arteriosus and even for the Aorta in the region of the ductus." Indigocarmine may act as an enzyme to reduce the increased Po$_2$.

A clinical demonstration of reduced blood pressure in presurgical testing is offered for placing renal responsibility.

Sincerely,

Hyman A. Levin, M.D.

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By The London Post

British National Health Services

Part VI

Ned Thomas

(This is the last of a series of six articles).

LONDON, England—Is England about to be bled white by the brain drain of its doctors?

"No! Categorically no!" asserts Oscar Gish, the leading authority on migration of medical manpower in Great Britain, when asked this question.

An American citizen, but currently a research fellow at the Science Policy Research Unit at the University of Sussex, Brighton, Mr. Gish noted that over the last 15 years some 7,000 British doctors have been lost through emigration to other countries.

This loss, Mr. Gish stated in an interview, has been more than made up numerically by the migration to Great Britain by other doctors, mainly from British Commonwealth nations.

During the past 15 years, the number of overseas-born doctors who have come to England has exceeded 10,000, more than making up the deficit of British-born doctors who left the country, he said. More have come and stayed in Britain than have left.

While acknowledging that the brain drain of British doctors, plus the loss of those foreign-born doctors who have returned to their native countries, has undoubtedly affected England's supply of medical manpower, Mr. Gish said it has not reached the point of endangering the country's National Health Service.

Based on a study done by the Science Policy Unit of Sussex University for the Education and World Affairs organization of Washington, D.C., Mr. Gish said that Britain has been benefitting from the inward migration of almost 2,000 doctors per year.

Some 500 to 600 of these doctors, he added, represent a net addition to the stock of overseas-born doctors already in the country. It is interesting to note, he said, that the 1,900 medical graduates who entered Great Britain in 1967, excluding medical school graduates who migrated from Ireland, were equal to the number of graduates of all British medical schools in that year.

The 2,000 figure for incoming foreign doctors, Mr. Gish said, is based on the number of work vouchers issued by the British Government. However, he has calculated that more than 200 doctors from old Commonwealth countries enter Britain annually without benefit of work vouchers.

To show how much Great Britain depends on foreign-born doctors, Mr. Gish said the National Health Service is employing 14,000 of them as junior doctors in hospitals. He said they represent 22 per cent of the total medical employment of the National Health Service.

About two-thirds of the foreign-born doctors in England come from India, Pakistan and Ceylon. They constitute a big majority of the junior doctors in the more populated areas of the country, and 51 per cent for the country as a whole.

In addition, there are in the country between 4,000 and 5,000 senior hospital staff and general practitioners who were born abroad.

Mr. Gish said that most foreign doctors come to Britain to further their careers and gain experience in sophisticated medical techniques. Some have found England to their liking and have stayed to practice medicine, but most leave eventually to return home.

Despite the "tremendous pressure" on British political leaders to curtail non-white immigration into the country, Mr. Gish said, the British Government continues to permit an increasing number of overseas medical graduates to come in for employment in the National Health Service. The reason for this, he explained, is Britain's "own critical need for them."

Currently, there is about one doctor for each 800 persons living in Britain, which is slightly less proportionately than exists in the U.S.

However, because of the National Health Service, medical care is more evenly spread throughout Great Britain than it is in the U.S. Whereas specialist doctors were formerly concentrated in London,

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MR. NED THOMAS is a science medical writer for the New Haven Register on leave.

they are now more equitably distributed throughout the country.

Is dissatisfaction with the National Health Service principally responsible for the fact that some 7,000 British doctors have migrated to the U.S., Canada and Australia during the past 15 years?

Mr. Gish indicated that while this may account for some of the doctors leaving, there are other factors that influenced many of them to leave.

He explained that the brain drain is an international phenomenon in which increasing numbers of highly qualified people have been moving from less to more developed countries in recent years. He added that this movement "has been encouraged" by the new American immigration laws which have made the possession of a skill "a major criterion" for entry into the U.S.

Medical doctors do not constitute the only group from England and the developing countries to migrate to the U.S. in recent years. Also among them are other high level manpower groups, including various scientists, engineers, technologists and other kinds of professionally trained personnel.

During the fiscal year of 1967, some 32,000 such persons entered the U.S., with more than half of them coming from developing countries.

"Virtually all countries," stated Mr. Gish, "are involved in the international game of beggar thy neighbour, with regard to skilled personnel. Some countries lose very few people while gaining many; others only lose people and gain none.

"Britain is one of those countries which experiences large movements in both directions—in and out. This is particularly true in the cases of doctors."

(It might be noted that despite the migration of doctors into the U.S., it was reported last year that there was a shortage of between 50,000 and 100,000 doctors in the country.)

Among the reasons for junior British doctors leaving England is the fact that some of them feel that there are greater opportunities for them to advance more quickly beyond the status of junior doctor in places like the U.S., Canada and Australia, where the need for more doctors is great. Undoubtedly, the promise of more money for their services has lured some of the doctors, too.

Mr. Gish also mentioned other reasons for the present shortage of British doctors. He said that between 1953 and 1968 the British medical schools had actually decreased the number of students that they normally trained. This resulted in a loss of 2,700 doctors who might have helped close the gap.

The emigration of the 7,000 British doctors in the last 15 years, Mr. Gish observed, has further "exacerbated that shortage and made it critical."

To help relieve the shortage of doctors, Great Britain has embarked on a program to double the output of its medical schools over what it was in 1965. It hopes to achieve this goal by the end of the next decade.

Observing that while some British doctors are always likely to be drawn to the more prosperous countries such as the U.S. and Canada, Mr. Gish asserted, "there is something wrong with the structure of the National Health Service when so many emigrate."

Insisting that this can be remedied, Mr. Gish proposed in a paper he wrote for the Institute of Race Relations that England's hospitals institute a modern staffing structure which will change its traditional apprenticeship pattern.

The current structure, he noted, is characterized by low wages, long hours and too few opportunities for junior doctors of advancing up the career ladder to better positions. Steps must be taken to correct these injustices and inequities to make jobs more attractive for gifted and ambitious junior doctors in the hospitals, Mr. Gish suggested.

"Without this and other needed changes," Mr. Gish stated, "it will prove difficult to keep young British doctors in the country."

From the

Connecticut Regional Medical Program

Henry T. Clark Jr., M.D., Director

What is the genesis of programs approved by the Connecticut Regional Medical Program? Who develops them? And what is the process for evaluating, approving and monitoring the programs?

The bulk of the programs currently in operation are the product of nine state-wide Task Forces and numerous subcommittees which examined Connecticut's health needs in the 20-month period ending March 1, 1968. Their studies focused on significant health problems with state-wide significance. Task Force recommendations to meet the identified needs were developed into proposals for operating programs which comprised the March 1, 1968 Operating Grant Request and the November 15, 1969 Continuing Grant Request. Many of these proposals were approved in Washington and are in operation with support from the basic CRMP grant of $1,320,750 for 1970.

The Challenge Grant Request submitted to Washington on April 27, 1970 represented another dimension in program development. Some of the proposals in the Challenge Grant package were an expansion of programs started in 1969, others were spell-outs of activities projected in the March 1, 1968 grant request. The various proposals demonstrated local initiative in seeking a solution to a recognized local health need while, at the same time, working toward fulfillment of CRMP objectives. CRMP hopes to obtain up to $330,187 to launch these activities during the second half of 1970.

The proposals were presented to CRMP by an individual, with the endorsement of the sponsoring agency, and, with staff assistance, shaped into an application for an operating grant. Occasionally, a local proposal was stimulated by the staff.

Examples of local initiative are present. Funds were requested to assist in the following: plan an ambulatory care service area, establish an office at Yale to catalyze allied health manpower development in Southwestern Connecticut, activate a coronary care nurse training program for staff members of Meriden-Wallingford, World War II Veterans Memorial, and Bradley Memorial Hospitals. All three proposals were developed by physicians, administrators and other health personnel working jointly and in harmony with CRMP objectives. All will be operational in 1970.

The steps in processing an application are as follows: the sponsoring agency develops the proposed program in accord with specific criteria and with CRMP staff consultation. When feasible, a technical advisory committee comments on the proposal while it is being formulated. It then goes from core staff to the CRMP Review and Evaluation Committee for consideration of its scientific merit, relevancy to CRMP goals, feasibility, regional significance, and ability of the applicant to carry it out.

Next it is evaluated and acted upon by the CRMP Executive Committee and then by the full 40-member Advisory Board. Finally, with the Board's recommendations and comments, it is forwarded to the Regional Medical Programs Service in Washington for study and action.

CRMP criteria for endorsement of a local application are:

1. The proposed program should contribute in a significant way toward implementing the CRMP grand strategy, which seeks to promote the best possible medical care to Connecticut's 3 million citizens in the most efficient way.

2. It should focus on an important health problem of local or regional significance and present a practical approach to the study and/or resolution of the problem.

3. It should have the potential for duplication in, or extension to, other parts of Connecticut.

4. Capacity for early implementation by the applicant must be clear; approval of the authorative body of the applicant agency is required, and responsible leadership for the program should be identified.

5. Any matching funds or resources available to undertake the activity must be documented.

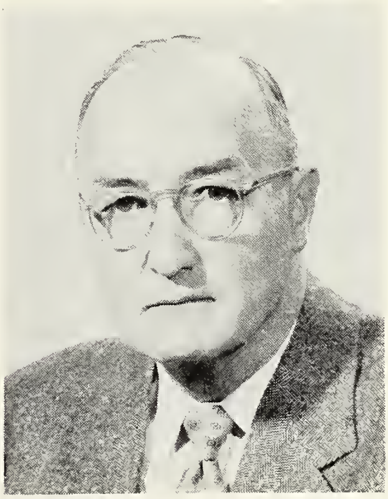
Local control of the program during its lifetime is firm. However, continuing staff consultation with the implementing agency and Advisory Board annual review of the progress of each program are requirements for continued sponsorship.

OBITUARY

Charles Christopher Wilson, M.D.

1895-1970

Dr. Wilson died suddenly from a heart attack on April 9, 1970, at the age of 75, following a busy, happy, and useful life, and 33 years after an earlier cardiac disability, that confined him in bed for many weeks.



Charlie Wilson, to his professional colleagues of the United States, was known as Chris to his family and close friends. He was a graduate of the Yale University School of Medicine in 1928; a member of Phi Chi medical fraternity, and of the Connecticut State Medical Society. His son, Charles S., a physician in Tenafly, New Jersey, is also a graduate of Yale.

Dr. Wilson's career was a somewhat unusual illustration of constructive service for people, especially for children of school age and their parents. Graduating from Springfield College, with a major in health and physical education, he taught for several years at Hartford High School before entering medical school. After graduation from medical school, he was director of health in the Evansville, Indiana public school system for six years, and then was called back to Hartford in a similar position—director of health and physical education, 1934-1941. He became Professor of Health Education and Chairman of the Department of Special Education at Columbia University Teachers College, 1941-1946. Then he was appointed Professor of Public Health and Education at Yale University, retiring in 1964.

From 1933 to 1945, Dr. Wilson was a member of the Joint Committee on Health Problems in Education for the National Education Association and the American Medical Association. As a member of the Advisory School Health Committee of the Connecticut State Department of Education, he led in the development of a report on school health policies which later received national recognition and adoption in adapted form. He was a nationally prominent leader in school health education and practices; and received the William A. Howe Award in 1953 in recognition of his contribution to the health of school children. He was the author of several publications for the joint committee of NEA and AMA, and of numerous articles in scientific publications, besides being a joint author with his wife, Mrs. Elizabeth Avery Wilson, of a series of textbooks entitled, "The American Health Series."

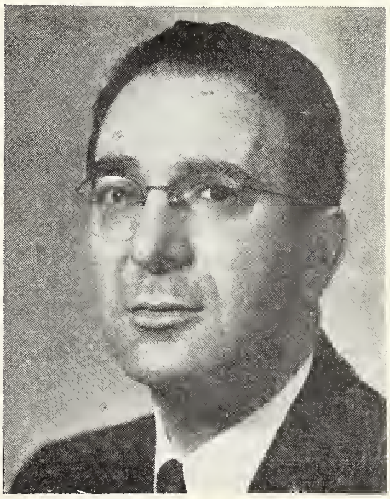
Dr. Wilson served as a consultant for various state departments of health and of education throughout the United States, and for the World Health Organization in South America and Europe. He resided at 50 Hawley Road, Hamden, Connecticut, where he served for a period on the local board of health.

Ira Vaughan Hiscock, M.P.H., ScD.

Jacob A. Segal, M.D.

1903-1970

Dr. Jacob A Segal, of Manchester, Connecticut, died on April 7th, at the age of 67, after a long illness.



Dr. Segal was born in Boston, January 3, 1903. He graduated from Tufts College in 1924, and from Tufts Medical School in 1928. His internship and residency training were at the Carney Hospital in Boston, Essex County Contagious Hospital in New Jersey, and Norwich State Hospital in Connecticut. From 1931-1941 Dr. Segal practiced in Framingham, Massachusetts, before moving to Manchester, Connecticut where he lived and worked.

Since 1942 Dr. Segal held various appointments on the medical staff of the Manchester Memorial Hospital. In 1955 be became chief of cardiology, a position he held until his death. Dr. Segal was past president of the medical staff of the Manchester Memorial Hospital, the Manchester Area Heart Association, and the Manchester Medical Association. He was a Fellow of the American College of Cardiology and of the International College of Angiology, and a member of the American Medical Association, Hartford Medical Society, Hartford County Medical Association, and the Connecticut State Medical Society.

He served with distinction in his hospital appointments, and was instrumental in organizing the electrocardiography department and the cardiac clinic at the hospital. In spite of a busy practice, Dr. Segal found the time and interest to contribute several original articles in cardiology which appeared in *Connecticut Medicine* and in 1961 was listed in *American Men of Medicine*. His role as a teacher and vital contributor to the health care of his community will be sorely missed by his fellow physicians and patients.

Dr. Segal is survived by his wife, Mrs. Frances Dembo Segal, two sons, Dr. Robert J. Segal and Attorney Joseph Segal, two grandchildren and a sister.

Martin Duke, M.D.

In Memoriam

Fabricant, Milton W., New London, Hahnemann Medical College 1939. Dr. Fabricant was a general practitioner in the New London area since 1947. He served as a major in the Army Medical Corps from 1941-1946. Dr. Fabricant was a member of the New London County Medical Association and the Connecticut State Medical Society. Dr. Fabricant died April 15, at the age of 58.

Flanagan, Edwin D., Clinton, St. Louis University School of Medicine 1935. Dr. Flanagan was a general practitioner in the Clinton area since 1955. He was the town's medical examiner and health officer. Dr. Flanagan served as a Lieutenant Commander in the U.S. Navy during World War II, 1944-1946 and served in the Pacific. Dr. Flanagan was on the staff of the Middlesex Memorial Hospital. Dr. Flanagan was a member of the Fairfield County Medical Association, American Medical Association and the Connecticut State Medical Society. Dr. Flanagan died April 10, at the age of 61.

Smith, Arthur C., Danbury, University of Maryland 1910. Dr. Smith was a general practitioner in the Danbury area since 1913. He had retired in 1959 after more than 46 years of practicing in Danbury but remained on the staff of Danbury Hospital as an honorary (inactive) member. He was the New Haven Railroad's surgeon for the Danbury area from 1918 until his retirement and also served the city as police surgeon and the town as town physician. He served 10 years as a trustee of Fairfield Hills Hospital, Newtown. In May 1963, Dr. Smith was honored by the Connecticut State Medical Society at a Hartford dinner for his 50 year membership. Dr. Smith was a member of the Danbury Medical Society, Fairfield County Medical Association, Connecticut State Medical Society and a fellow of the American Medical Association. Dr. Smith died April 25, at the age of 84.

Wilson, Frank E., Wethersfield, University of Vermont 1911. Dr. Wilson was an ophthalmologist. He served in the U.S. Army. Dr. Wilson was a member of the American Medical Association, New London County Medical Association, Connecticut State Medical Society and the Board of Academy of Ophthalmologist and Otolaryngology. Dr. Wilson died May 3, at the age of 82.

Consortium To Fight Dirty Air

(*Science* 167: 359, Jan. 23, 1970) Three North Carolina universities have joined forces to fight air pollution in the nation's first academic clean air consortium. Duke University, The University of North Carolina at Chapel Hill and North Carolina State University plan to offer comparative courses, workshops, seminars, public meetings and technical conferences.—L.H.N.

WOMAN'S AUXILIARY

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A streamlined, informative program with ample time for fun, renewing old friendships and making new friends will be held at the Drake Hotel. You are cordially invited to a reception honoring the National President and President-elect, Sunday, June 21. The Convention opens formally Monday, June 22, with the keynote address to be given by Mrs. Louise Bushnell, Program Director, Women's Activities, National Association of Manufacturers. Her theme will cover the Challenge to Women in the '70's. A "Nite on the Town" has been planned for Monday. Following the Tuesday luncheon a Pageant of costumes worn by women through the ages will tell the story of "Woman's Role Through the Ages". "Show and Tell" exhibits demonstrating activities of county and state auxiliaries will be another popular feature.

The Auxiliary will sponsor a program of daily activities for the pre-teens and teenagers of Auxiliary members. Complete details will appear in the May issue of MD's WIFE.

Mrs. John M. Chenault "hopes that our convention plans will appeal to you and that you will take advantage of the many opportunities to hear outstanding speakers, get current information on Auxiliary projects and enjoy social events".

Hotel Reservations: Rooms have been set aside for members of the Woman's Auxiliary at the Drake Hotel. Reservation forms appeared in the March issue of MD's WIFE.

That "Toddlin' Town," Carl Sandburg's "City of the Big Shoulders," Frank Sinatra's "My Kind of Town"—Chicago is waiting to welcome you for the 47th Annual Convention of the Woman's Auxiliary to the American Medical Association, June 21 to 25.

Headquarters for the AMA Woman's Auxiliary is the elegant Drake Hotel on Chicago's lakefront. Delegates and guests may register daily Sunday through Wednesday.

Ever since the days when the 350 souls living at the junction of the Chicago River and Lake Michigan provided hospitality for wayfarers moving westward, Chicago has had the reputation for knowing how to entertain. Sightseeing, theatre, sports, shopping, nightlife, more than 135,000 first-class hotel rooms—Chicago has them all.

Auxiliary events get under way on Sunday, June 21, with a reception from 5 to 7 P.M. honoring the auxiliary's president and president-elect. At the Monday luncheon honoring AMA officers, trustees and their wives, the speaker will be Gerald L. Dorman, M.D., 1969-70 AMA president. At the Tuesday luncheon, a unique fashion show will tell the story of "Woman's Role Through the Ages" (MD's WIFE, January 1970).

"Show and Tell," featuring exhibits of state auxiliaries, which was well received last year, will again be on the convention schedule. Ample time will be allowed for browsing. The installation of Mrs. R. C. L. Robertson of Houston, Texas, as 1970-71 president will take place on Wednesday.

A block of rooms has been reserved at the Drake Hotel for auxiliary members. Make your reservations as soon as possible, using the official form below.

The AMA Woman's Auxiliary once again is planning an exiciting schedule of activities for pre-teens and teenagers during the annual convention in Chicago. The program will be handled by Gulliver's Trails. We know you will not want your youngsters to miss the events which include an opening night dinner-theatre performance at famed Pheasant Run Playhouse in St. Charles.

All programs are planned so that pre-teens and teenagers will travel in their own groups. Registration will be on Sunday, June 21, at the Drake Hotel and all pick up and returns will be at the Drake. Please make reservations in advance, using the form below.

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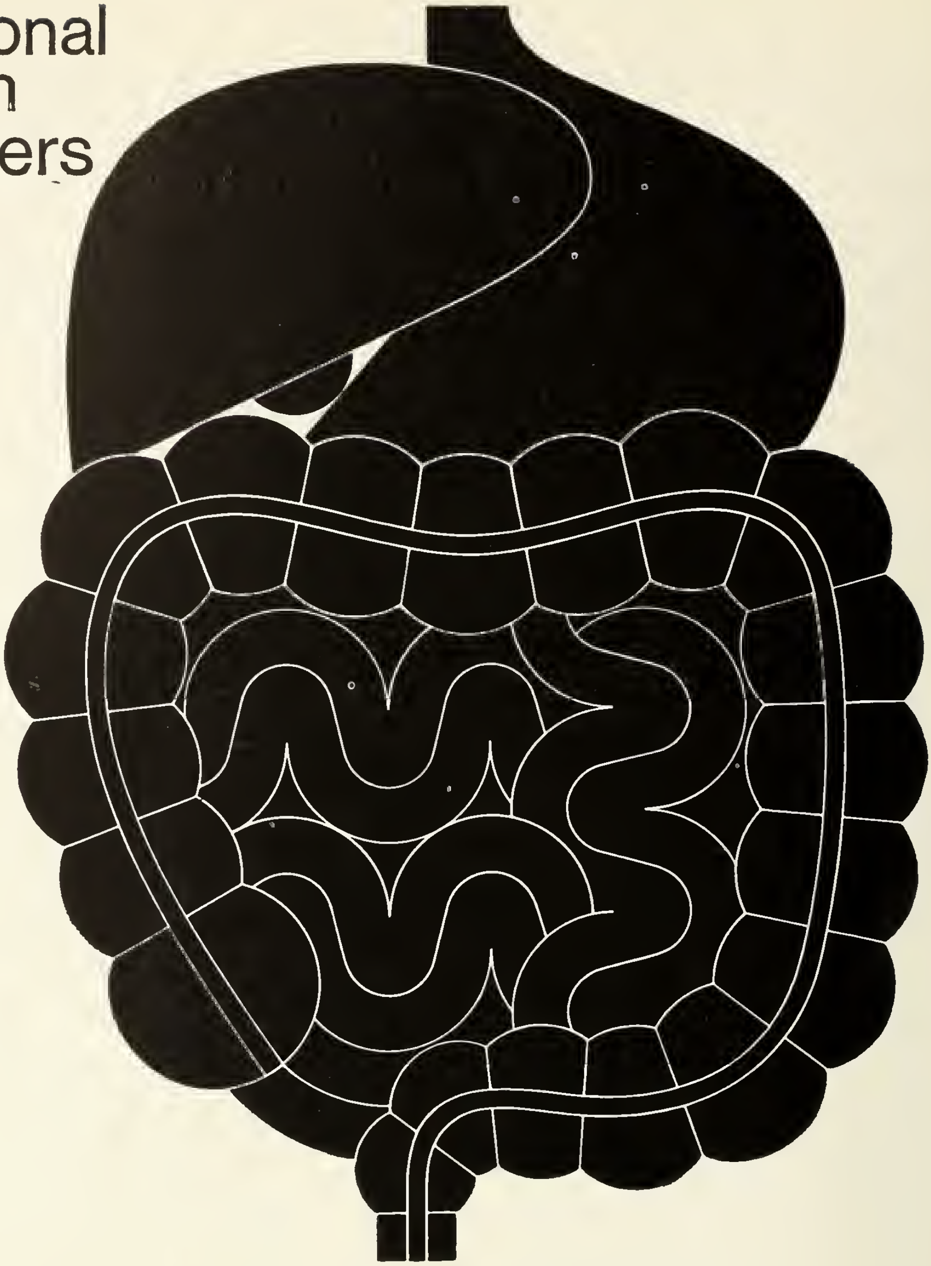

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Monday, June 22

Boat Ride and Museum of Science and Industry. Pre-Teens (6-12) and Teens (13-17). 9:30 A.M. to 4 P.M.). Take a two-hour boat ride around Chicago on Lake Michigan and the Chicago River. Bring cameras to snap highlights of the beautiful Chicago skyline. On to Shedd Aquarium and then lunch and the afternoon at world-famed Museum of Science and Industry. Tour a coal mine, make a TV phone call, go aboard a U-505 submarine and explore other unique areas of this fabulous museum. Price with lunch: $12, one child; $10.50 each for two or more children.

Tuesday, June 23

Swimming, Sightseeing and Opening Night Theatre Party. Pre-teens and Teens. (12:30 P.M. to 11:30 P.M.). A day and evening at the famed Pheasant Run Playhouse in St. Charles. Enjoy an indoor-outdoor swim party, browse in a recreated village of Bourbon Street, watch the horseback riding ring and then have dinner and attend the opening night performance of a top comedy with star performers. Note for pre-teens—for those who may not want to attend the theatre, arrangements may possibly be made to return in the early evening for dinner and a movie in Chicago. Price with dinner and theatre: $16.

Wednesday, June 24

Brookfield Zoo, Porpoise Show and Newspaper Tour. Pre-Teens. (9:30 A.M. to 4:30 P.M.). Visit one of the country's top newspapers, then a picnic lunch, a porpoise show and an afternoon at exciting Brookfield Zoo where the animals roam free as they do on the African preserves. Price: $12, one child; $10.50 each for two or more.

Newspaper Tour, University of Chicago. Teens. (9:30 to 4:30 P.M.). A visit to the famous *Chicago Tribune* where you'll see a film, "Big City Paper," then tour the news and production departments. Then on to the University of Chicago where university students will give you a guided tour. Lunch on the campus with the students, then a guided tour of the Chicago Board of Trade. Price with lunch: $12, one child; $10.50 each for two or more.

Thursday, June 25

Marina City, the Lincoln Story and the Police Academy. Pre-teens and Teens. (9:30 A.M. to 4:30 P.M.). Start with a visit to the world's tallest apartment house, the 60-story, round Marina City. Lunch in Chinatown, then a tour of the Chicago Police Academy. Price with lunch: $12, one child; $10.50 with two or more.

News From Yale University School of Medicine

Dr. Joseph R. Bertino of the Yale School of Medicine received the 1970 award for experimental therapeutics from the American Society for Pharmacology and Experimental Therapeutics.

Dr. Bertino was cited for his basic work in the chemotherapy of leukemia. He is Professor of Medicine and Pharmacology and Chief of the Section of Oncology and Chemotherapy at Yale.

His work, for which he received the award, is focused on the molecular mechanism by which certain drugs, in particular methotrexate, inhibit key enzymes, resulting in the death of leukemic cells.

Methotrexate, a frolic acid antagonist, tightly binds dihydrofolate reductase, a key enzyme in the synthesis of Deoxyribonucleic Acid (DNA), the genetic material of cells. Cells that can't replicate DNA then die.

Dr. Bertino's study of the molecular mechanisms of action of this therapeutic agent have led to increased understanding of the fundamental processes by which methotrexate arrests acute leukemia in children and favorably affects some other malignant diseases.

By administering leucovorin (folinic acid), which is converted to reduced folate, the end product of the reaction inhibited by methotrexate, Dr. Bertino has demonstrated in patients that normal cells can be protected and tumor cells attacked. Since the bone marrow and intestine of patients—the usual sites of unfavorable toxicity—can be protected in this fashion, high doses of methotrexate can be safely administered.

The clinical and basic approaches in Dr. Bertino's work have been used to devise predictive tests, new treatment schedules and new combination therapies for the treatment of human malignancies.

Dr. Bertino was appointed Assistant Professor at Yale in 1961, Associate Professor in 1964, Chief of the Section on Oncology and Chemotherapy in 1966 and Professor, without term, in the Departments of Medicine and Pharmacology in 1969.

He is a member of the Chemotherapy Advisory Committee, National Cancer Institute; National Medical Advisory Board, Leukemia Society of America; and a past Chairman of the Experimental Therapeutics and Pharmacology B study section. He is also an editor of Molecular Pharmacology.

LABORATORY NOTES

ROY N. BARNETT, M.D., Norwalk Hospital, Norwalk, Conn.

Blood Gases and Acid Base Balance

Knowledge of blood pH, PCO_2 and PO_2 permits certain deductions about acidbase and respiratory status such as:

1. *Base excess* (+BE, mEq/L) a measure of metabolic alkalosis, or

2. *Base deficit* (—BE, mEq/L) a measure of metabolic acidosis.

These terms, popularized by Siggaard-Anderson replace "Buffer Base".

3. % *O_2 saturation* of Hemoglobin. This depends on PO_2 and PCO_2 because CO_2 may displace some O_2 when PCO_2 is high.

On request the Clinical Pathologist on call will issue a *Blood gas acid-base report form including*

1. measured pH, PO_2 and PCO_2
2. Base excess or deficit
3. Interpretation of metabolic disturbance
4. Calculated dose of IV solution to correct the metabolic component
5. % O_2 saturation
6. Modified Kintner diagram to graphically display PCO_2 and bicarbonate disturbances. This helps indicate the need for IV fluids or respiratory aids.

Use of venous blood

Many acidbase disturbances are adequately studied by venous blood analysis. When there is no severe circulatory disturbance venous pH is .03 or less lower, PCO_2 6 mm or less higher, and BE 2.5 mEq/L or less higher than arterial blood.

Specimen required

5 ml of heparinized arterial or venous blood. Capillary blood—consult pathologist.

Also send patient's weight and hemoglobin.

I. Weisbrot, M.D.

Test for Opiates

After a considerable struggle we have now settled on a satisfactory TLC (thin-layer-chromatography) method for detecting the following drugs in urine:

Morphine (heroin appears in the urine as morphine)

Codeine

Quinine (often used to "cut" drugs).

This is a qualitative but very sensitive method and can be performed on 50 ml of a random specimen. We are working on tests for other substances such as barbiturates, amphetamines, etc.

IV Solutions are not Chicken Soup

Chicken Soup, an important therapeutic agent, can be improved by adding small dabs of spices, herbs and vegetables. Exact quantitative measurements are unnecessary and each cook can make his own variations.

IV fluids are different. They should be kept as simple, as pure and as free of extras as possible. Why?

1. Dangerous precipitates may be produced by additives. They may be difficult to see and may not develop at once.

2. Different active ingredients may require different rates of flow. The rate of antibiotic administration in a mixture with antihypotensive agents is governed by the blood pressure rather than by the infection, and this makes no sense.

Proper solutions recommended by manufacturers are listed in "Instructions to the Wards" on each floor; also in IV and Pharmacy. Manufacturers do not list all the incompatibilities.

We urge you to use only the recommended mixtures for everyone's protection. Come see our museum of precipitates in the IV Dept.

Iron in Feces

Do you ever wonder whether your patient is really taking his (her) iron tablets? A simple test of the feces will give a definitive answer (Gambino, 1969). Order as "Iron in feces".

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Science News

Heart Murmurs May Be Masked By Pregnancy

(*JAMA*, 210: 1841, December 8, 1969) Murmurs of aortic and mitral regurgitation—clues to rheumatic heart disease and valvular disease—can become so faint in pregnant women that they may be overlooked, according to a study reported at the American Heart Association meeting in Dallas.

Pregnant women with these heart conditions are susceptible to bacterial endocarditis at the time of delivery, said Frank I. Marcus, M.D. Dr. Marcus, who headed the study, is professor of medicine at the University of Arizona College of Medicine.

"Organic heart disease must be suspected during pregnancy when there is a history of rheumatic fever or rheumatic heart disease, even in the absence of the murmur of aortic or mitral valve regurgitation," Dr. Marcus recommends.

He added that physicians should also listen for the murmurs after the termination of pregnancy.

Allan C. Bleich, M.D., now of the Emory University School of Medicine, Atlanta, presented the report based on a study of 26 pregnant women examined at various Washington, D.C., and Atlanta hospitals over a five-year period.

Women chosen for the study were asymptomatic but had histories that suggested heart disease. Each woman was examined by the same physician during pregnancy and either before or after pregnancy. Some of the patients had both aortic and mitral valve incompetence.

In 9 of 16 patients with aortic incompetence, the murmur could not be heard during pregnancy but was audible during examinations when they were not pregnant. The intensity of the murmur remained the same in four women and decreased in two. In one woman who became hypertensive during pregnancy, the murmur increased in intensity.—L.H.N.

Immunization Against Rubella

(J. A. Dudgeon: *Nature*: 223, 674, August 16, 1969) German Measles can cause congenital malformation, often severe and frequently multiple. Techniques are now available for accurate diagnosis and the development of a vaccine. In the future it should be possible to prevent rubella during pregnancy.

Vaccines are attenuated but their effects on the fetus is not known and they should not be given during pregnancy. Until more is known about the length of immunity following rubella vaccines it would be premature to make a firm decision on the optimal age at which immunization should be introduced. There are two possibilities.

First immunization in infants and young children may be introduced with the ultimate object of eradicating the disease. Second the alternative approach may be used of immunizing older children particularly girls before puberty.—L.H.N.

Herpes Globulin Prevents Varicella

(*JAMA*, 208: 2001, June 16, 1969) Dr. Philip A. Brunell prepared immune globulin from plasma of donors recovering from herpes zoster infection since herpes zoster and varicella are caused by the same virus. He then gave it to children exposed to varicella within 72 hours after exposure. None of the children who received the immune globulin contracted varicella. The dosage required was 0.05 to 0.07 ml. per pound of body weight. The minimum amount may be less and studies are underway to determine this as well as the adult dose.—L.H.N.

Heart Transplants

(*Science*, 167: 359, January 23, 1970) A report to the National Heart and Lung Institute by an 11 member task force headed by Dr. James V. Warren recommends that researchers concentrate on perfecting human heart transplants and on developing heart arrest devices including wholly artificial hearts.

Even with the donor and rejection problem solved, there still remains the lymphatic drainage problem. However, most heart victims cannot be saved because 40 or more percent die suddenly or because they have other serious diseases. With the three problems solved transpants could be performed on 16 percent of the 200,000 Americans under age 65 who die each year.

The report recommends strong federal programs for the prevention and early detection of heart disease.—L.H.N.

Nerve Gas Tests Suspended

(*Science*, 167: 359, Jan. 23, 1970) The army has suspended temporarily its open-air tests of lethal chemicals at the Desert Test Center (Proving Grounds) Utah. According to an army official the suspension was ordered because of an amendment to the procurement bill for 1970. The amendment named after Senator Thomas McIntyre (D-N.H.) sets new requirements for testing chemical and biological warfare materials.

The requirements include a provision that Congress be given a schedule of tests prior to any testing, and that the Secretary of Defense consult the Secretary of HEW and the Surgeon General, prior to testing to ensure adequate safeguards.

The Army expects to have complied with these requirements in a few weeks and *will resume tests then.*—L.H.N.

Microwave Ovens

(*Science* 167: 359, Jan. 23, 1970) A government industry consumer committee will be formed promptly to set up test procedures and develop testing programs for microwave ovens, the Department of H.E.W. announced recently.

The ovens are suspected of leaking high-frequency radiowaves. Such leakage in excess of the industry's voluntary standards was detected in nearly one-third of the microwave ovens tested in four states by H.E.W.

About 1000,000 microwave ovens are in use in American homes and institutions. H.E.W. officials said there have been no reports of injuries from oven owners and that any defects found in the ovens will be corrected.—L.H.N.

Chlorotic Dwarf Of Eastern White Pine Caused By An Ozone And Sulphur Dioxide Interaction

(*Nature*, 225: 476, Jan. 31, 1970) Dochinger, L. S., et al. This disease is characterized by stunted roots and tops, mottled needles and premature foliar abscission. These authors have shown that the disease is caused by gaseous pollutants that injure the needles of genetically susceptible white pines.

Now they show that the action and interaction of ozone and sulphur dioxide is what causes the characteristic symptoms on the foliage of white pine that are susceptible to chlorotic dwarf. Thus not only humans are affected by sulphur dioxide producing increased atherogenesis, but trees as well.—L.H.N.

Packaging Pollution Control Act of 1970

(*Science*, 168: 232, 1970) Senator Gaylord Nelson has introduced a bill that would levy a "solid waste fee" on industries for product packaging according to several criteria including the possible toxic and health effects of disposal of the package and the ease with which the package could be "recycled." The Packaging Pollution Control Act of 1970 directs the HEW Secretary and the Secretary of the Treasury to make a schedule of national packaging charges that reflects the effect of each type of packaging upon the environment. The bill proposes that the national packaging charges be routed to state and local governments for the construction and expansion of solid waste facilities.—L.H.N.

General Practitioners And The District Hospitals

(*British Med. Jr.*: Vol. 1, Jan. 3, 1970) General practitioners in Great Britain unlike many colleagues overseas do not normally enjoy direct access to beds in major hospitals. They, however, are fighting for this privilege.

It may be unrealistic that general practitioners can or will always want to make more than a marginal contribution to staffing hospital service. A better participation, however, may come in situations where the family doctor can offer the hospital staff team a skill based on his special knowledge and experience in environmental and psychosocial factors in the patient's illness.

This skill could bring him into contact with all clinical specialties in hospitals. His advice would be sought and given in the spirit of one expert to another.—L.H.N.

Sterile Males For Control Of Insect Populations

(*Science*, 168, 163, April 3, 1970, LaChance, Leo E.) Conference on Sterile Male Technic for control of insects with Special Reference to Fruit Flies was held in Vienna, Austria, Sept. 1-5, 1969. Flies were laboratory reared and sterilized. Thus liberation in appropriate amounts led to reduction of damage to fruit from 90-100 per cent down to 10 per cent.

The successful results in several field trials with the medfly were promising enough to warrant a large scale demonstration experiment for the control or eradication of this species over a large area. Both development and progress of the sterile-male-release method for a number of other species of fruit flies were promising enough to justify small-scale field trials.

A proposed plan to eradicate the medfly from Nicaragua was presented. Some of the obstacles hampering the application of this method to other fruit flies were (1) development of economical, large-scale mass-rearing techniques, (2) difficulties in mass release of sterilized insects, (3) dearth of ecological information on the distribution of fruit fly species in various countries.

Several solutions to these problems were proposed, and coordinated research programs were discussed.—L.H.N.

Dietary Sucrose And Platelet Behavior

(*Science,* 225: 467, Jan. 31, 1970) Szanto, S. Yudkin, J. Platelet adhesiveness is now known to play a role in arterial thrombosis. A diet rich in sucrose causes in young men an increase in body weight, in plasma insulin levels, and in platelet adhesiveness.

The authors now report their observations on three subjects previously shown to develop sucrose induced hyperinsulinism and three subjects shown not to do so. At the beginning of the study the platelet mobility of both groups of subjects was the same. At the end of the period of high sucrose diets, the subjects with hyperinsulinism showed a change in platelets to that present in atherosclerosis.

The plasma of these subjects could change the behavior of normal platelets to that found in atherosclerosis. The factor in such plasma is not known. One possibility is that the abnormality produced by dietary sugar was a direct result of the higher insulin level in the plasma. This is probably not so for the factor remained after insulin levels became normal. Furthermore, poreine insulin did not affect the platelet behavior. The next step is to determine what the factor really is.—L.H.N.

Is There A Photographic Memory (Eidetic)

(*Nature,* 225: 227 January 17, 1970) Leask, et al define eidetic image as a visual image of a figure usually long in duration localized in space in front of the subjects "eyes". To each of 531 school children they first demonstrated after-images such as results from staring at a lamp bulb. All children reported seeing after images. Next each child was shown a series of pictures. After inspecting it for 30 seconds, actively scanning it with his eye, a child described what he saw on a grey screen on which the picture had been placed.

Only 35 children were classified as eidetic. These claimed that they were not simply remembering what had been seen in the picture. Their reports were of a vivid image "out there" in front of them.

Some of the eidetic children who were tested between age 7-14 were retested at intervals of 5 years. There was no decrement of eidetic imagery as they grew older. However, to obtain a good image the eidetic child had to concentrate on it.

The problem of being certain that a subject has eidetic imagery is a real obstacle to research. Some believe "the eidetics amazing accuracy is not amazing at all and probably well within the range of normal memory". The eidetics, however, may be the artists of the future and should be identified.—L.H.N.

Pituitary Growth Hormone Essential For Regulation Of Serum Cholesterol

(*Nature,* 225: 464, January 31, 1970) Friedman, M., Byers, S. O., Elek, S. R. Hypophysectomized rats develop hypercholesterolemia. The question is whether this is due to impaired thyroid function, other glands regulated by the pituitary or to growth hormone deficiency.

A careful controlled study by the authors led them to conclude that hypercholesterolemia taking place in the hypophysectomized rat was not the result solely of thyroid hypofunction and was probably totally independent of the sex and adrenal glands. Some other hormone was involved. They identified it finally as the growth hormone after numerous experiments.

They found that physiological doses of thyroid and normal doses of growth hormone is necessary for a normal cholesterolemic status.

This effect of growth hormone has in the past been obscured partly by the fact that it has usually been administered to normal animals in too large doses. In acromegalics the effect of growth hormone is obscured by diabetic complication. When this is controlled, however, the hypercholesterolemic state disappears. Growth hormone certainly is an important regulator of plasma cholesterol levels.—L.H.N.

New Angle On Car Collisions

(*Nature,* 225: 228, January 17, 1970) Collisions at an angle of impact of less than 45 degrees rarely produce enough rotational motion to lessen significantly the impact of drivers on the windscreen or its supports. Seat belts are extremely valuable even in many oblique angle collisions.

Grimes and Jones considered many classes of collisions including head on, side on, asymmetrical head on and oblique angle side on known as "sideswipe". Their purpose was to present design engineers with sample mechanical models of car crashes which can be analyzed to determine situations in which seat belts are not the complete solution.

Several interesting points are put forward. One is to design vehicles to favor deliberately passengers wearing seat belts. Strengthening the side of the vehicle is also important.

Although seat belts have been found to reduce serious injury by about 50 percent, nevertheless, not all people wear them and attempts to devise other forms of safety device are under way which are less optional such as air cushions and reinforced doors. —L.H.N.

DOXEPIN (SINEQUAN) AND OTHER DRUGS FOR ANXIETY AND DEPRESSION

Almost everyone experiences occasional anxiety or mild depression of brief duration, and drug therapy for these conditions is seldom needed. Moderate to severe depression often associated with anxiety and of variable duration is a common symptom of psychoneuroses, manic-depressive, involutional, and reactive phychoses, schizophrenia, and other functional and organic mental disorders; for these conditions, drug therapy is often needed.

Trials with Antianxiety and Antidepressant Drugs

Sedatives such as the barbiturates and the benzodiazepins (chlordiazepoxide [Librium] and diazepam [Valium]) are useful in relieving anxiety, and the phenothiazines are often effective in patients with severe anxiety or agitation. How effective the antidepressant drugs are is difficult to determine from the conflicting results of many studies. The better the design of a trial of antidepressant drugs, the poorer the results have tended to be. In an analysis of the clinical data of 490 trials with antidepressant drugs published in 71 journals up to 1966 (A. Smith et al., Psychopharmacol. Bull., March 1969), well-designed studies were found to be few and in these the differences between the effectiveness of antidepressant drugs and placebo were not impressive. Nevertheless, many clinicians believe that the amphetamines are useful in mild depression and the tricyclic antidepressants in more severe depression.

Older Drugs

Some drugs are claimed to combine antidepressant and antianxiety properties. Merck, for example, claims that amitriptyline "has a tranquilizing component to its action which is particularly helpful in alleviating anxiety or agitation that often accompanies depression." Sandoz promotes thioridazine (Mellaril) as a single drug for "symptoms of mixed anxiety-depression. . ."; Roche claims that diazepam "helps relieve psychic tension with associated depressive symptoms." In addition to single drugs, fixed-ratio combinations of amitriptyline and a major tranquilizer, perphenazine (Trilafon), have been used for several years as Triavil (Merck) and Etrafon (Schering) for the treatment of moderate to severe depression accompanied by anxiety or agitation. Many clinicians have also used antianxiety or sedative drugs and tricyclic antidepressants together, varying the dosage of each component according to the changing clinical state of the patient.

Doxepin

Doxepin hydrochloride (Sinequan—Pfizer), a dibenzoxepin tricyclic compound structurally related to amitriptyline, is currently being promoted as "The first single agent with *potent* antianxiety and antidepressant action [which] . . . Can be prescribed as a tranquilizer, an antidepressant . . . or both." The manufacturer recommends the drug for a wide range of psychoneuroses and psychotic depressive disorders. Though it is not the first drug offered for both anxiety and depression, if it were in fact more effective against both symptoms than previously available drugs it would be a useful therapeutic advance.

Most of the studies on doxepin were reported at a symposium arranged by the manufacturer in December 1968; the reports appear in a special issue of Psychosomatics (Vol. 10, May-June 1969). Although a double-blind procedure was reported in most of the studies, the descriptions of the methods used leave unanswered so many questions about the quality of the design of the studies and the controls used that it is difficult to assess the value of the drug for either depression or anxiety. Furthermore, because of the imprecision of diagnostic categories relating to depression and anxiety, and disagreement among clinicians as to measurement of improvement as well as diagnosis, different trials are difficult to compare and the results of trials of antidepressant or antianxiety drugs can be accepted only with reservations.

Other Studies

E. E. Johnstone and J. L. Claghorn (Curr. Ther. Res., 10: 514, 1968) compared doxepin with chlordiazepoxide in two groups of 15 patients with psychoneurotic anxiety with depressive features, and concluded that doxepin was more effective as a tranquilizer than as an antidepressant, and for that purpose, was superior to chlordiazepoxide. On the other hand, in a study by K. Rickels et al. (Psychopharmacologia, 15:265, 1969) on patients with anxiety frequently accompanied by depression, it was concluded that doxepin, as compared with diazepam, produced more improvement in symptoms of depression than of anxiety. Evidence for its effectiveness in relieving anxiety or depression in organic disease, alcoholism, and manic-depressive psychosis is lacking.

Adverse Effects

Like other tricyclic drugs, doxepin can have anticholinergic effects and can cause hypotension and extrapyramidal symptoms. Drowsiness is frequent, and the manufacturer warns that patients should be cautioned against driving a car or operating dangerous machinery while taking the drug. The safety of the drug in pragnancy and lactation and for children under 12 years of age has not been established. All tricyclic antidepressants can antagonize the antihypertensive effect of guanthidine (Ismelin).

Dosage

The recommended dosage range is 25 to 300 mg a day in three divided doses. The manufacturer points out that as with other tricyclic antidepressants, antidepressant response may not be evident for as long as three weeks.

Conclusion

From a review of the published trials and from comments of Medical Letter consultants, it appears that doxepin has antidepressant and antianxiety effects in many patients, but that its superiority to other drugs for either symptom or for the combination of symptoms has not been established. It is a new drug and the full range of its adverse effects may not yet have become evident. For the present, when moderate or severe anxiety is the predominant symptom and depression is mild, a sedative drug such as a barbiturate, chlordiazepoxide, or meprobamate (Equanil; Miltown; and other brands) can be prescribed; for agitation, a phenothiazine can replace the sedative. When moderate to severe depression is the predominant symptom, a tricyclic antidepressant can be tried. Some patients seem to do better on one drug than on another. MAO inhibitors are less likely to be effective and have more serious adverse effects and interactions. When depression or anxiety is severe, psychotherapy as well as drugs may be needed. For moderately depressed patients who experience disturbing adverse effects from antidepressant drugs, a placebo given with positive expectations of improvement may be a useful alternative. Severely depressed patients may require electroconvulsive therapy. (The value of lithium in the prevention and treatment of manic-depressive states is discussed in The Medical Letter, Vol. 12, p. 10, Feb. 6, 1970.)

Tricyclic Antidepressants

Drug	*Usual Dosage Range*[1] *and Approx. Prices*	*Major Adverse Effects*[2]
Imipramine (Tofranil)	30 to 200 mg/day $0.29 to 0.96	*Frequent*: anticholinergic effects (dry mouth, etc.); hypotension; antagonizes the antihypertensive effects of guanethidine *Occasional*: drowsiness; hypomanic or manic episodes; cholestatic jaundice; extrapyramidal symptoms; first-degree heart block; allergic rashes *Rare*: bone-marrow depression including agranulocytosis; epileptiform seizures have been reported; peripheral neuropathy
Amitriptyline[3] (Elavil)	40 to 300 mg/day 0.29 to 1.56	
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[1] Usual frequency of administration is three times daily.

[2] Probably common to all tricyclcs. Frequency of adverse effects such as drowsiness varies with different drugs. MAO-inhibiting drugs should be discontinued at least two weeks before using a tricyclic drug.

[3] Sedative effects may be more frequent than with other tricyclic drugs.

Reprinted from *The Medical Letter on Drugs and Therapeutics*, New York, N.Y. Vol. 12, No. 5, March 6, 1970.

NEW BOOKS IN REVIEW

CARDIOVASCULAR SURGERY CURRENT PRACTICE, VOLUME 1. Edited by Thomas H. Burford, M.D., Professor of Clinical Thoracic and Cardiovascular Surgery, Washington University School of Medicine; Associate Thoracic Surgeon, Barnes Hospital and St. Louis Children's Hospital, St. Louis, Missouri and Thomas B. Ferguson, M.D., Associate Professor of Clinical Thoracic and Cardiovascular Surgery, Washington University School of Medicine; Attending Thoracic Surgeon, Barnes Hospital and St. Louis Children's Hospital, St. Louis, Missouri. The C. V. Mosby Company, St. Louis, 1969. 273 pp. with 134 illustrations. $18.00

Reviewed by: LOUIS H. NAHUM

In the early 30's Elliot Cutler Professor of Surgery at Harvard attempted to cure mitral stenosis by cutting the valve blindly through the atrium. Three patients died and the one survivor was later found not to have had the valve cut. It was the first surgical invasion of the heart. Robert Gross's successful case of a patent ductus did, of course, not involve invasion of the interior of the heart.

Now in this volume edited by Burford and Ferguson one can see the tremendous strides that have been made in the last two decades. The thirteen contributors are celebrated. There are nine chapters on heart lung machines, post operative care of general heart patients, treatment of Tetralogy of Fallot, artificial heart valves, myocardial revascularization, cardiac transplantation, and ventricular assistive devices present and future.

In the foreword Lord Brook expresses his opinion that this book is destined for complete success. Success in cardiac surgery is now possible because it is possible to open the heart widely, critically inspect the lesion, and perform definitive surgery. Thus the way is laid open for open-heart surgery. The advances can be proclaimed as brilliant and worthy. However, it will soon be out of date for total body perfusion and all its complications and problems associated with it must soon be replaced with a simpler and safer method.

Another problem to be solved is how to replace the present prostheses by more biologic methods. The undreamed of successes in the last 2 decades offers hope that these two desired advances are sure to come soon.

STUDIES IN CLINICAL ENZYMOLOGY. Edited by D.P. Mullan. The C. V. Mosby Company, St. Louis, 1969. 238 pp. $12.00.

Reviewed by: LOUIS H. NAHUM

The author has selected various clinical topics in enzymology which are primarily of interest to the general physician and describe the enzyme changes which occur. Certain sections of this book are also of interest to the obstetrician, pediatrician, neurologist and those interested in tropical medicine.

There are eleven chapters. The first on nature of enzymes and their diagnostic value. Then chapters on enzyme changes in heart disease, pregnancy, detection cervical carcinoma by enzymes, inherited metabolic and enzyme abnormalities, enzyme studies in diabetes mellitus, in urinary tract disease and hypertension and cerebro spinal fluid enzyme abnormalities. There are two chapters one on enzyme studies in African heart disease and another on imported tropical disease amoebiasis and other liver disorders.

The longest chapter is on enzyme changes in pregnancy. It is a practical book with much information of value to students and physicians.

CONTROVERSY IN OBSTETRICS AND GYNECOLOGY. Edited by Duncan E. Reid, M.D., and T. C. Barton, M.D. with 60 eminent contributors. W. B. Saunders Co., Philadelphia, Pennsylvania, and London, 1969. 414 pp., Illustrated. $15.50 U.S., $16.75 Canada.

Reviewed by: ORVAN W. HESS

This 400-page treatise on gynecological obstetrical subjects of major importance provides a vehicle for presenting the more or less individualized opinions of sixty well-qualified contributors. The title of the book immediately engages the attention and interest of the potential reader. As one might suspect, the subjects selected for discussion are those about which questions exist which have not yet reached a stage of complete resolution or universal agreement. In one sense, this book represents an extension of the kind of experience commonly encountered with the seminar or conference approach, albeit by participants of wide experience or special expertise, which frequently brings to light different viewpoints.

In recording alternative points of view, this book offers a stimulating and effective learning experience. This type of exposure to new research findings and the results of new forms of management of "long-standing problems" can be effective in lessening the tendency toward dogma in patient care. Topics range widely from ectopic pregnancy, threatened abortion and premature rupture of the membranes to a consideration of the anovulatory ovary and surgery versus x-ray in treatment of cancer of the cervix. The chapter on fetal distress is particularly significant in calling attention to the progress in our knowledge in our attempts to elucidate this important problem during the past decade. This advance has resulted largely from the application of newly developed electronic and biochemical techniques which are not only useful in monitoring fetal status but also have value in clinical management.

This book is highly recommended. It should be of interest not only to clinicians and students but to investigators as well.

MEDICAL LABORATORY TECHNOLOGY AND CLINICAL PATHOLOGY, July, 1969. By Matthew J. Lynch, M.D., Stanley S. Raphael, M.B., Leslie D. Mellor, Peter D. Spare, and Martin J. H. Inwood; 2nd Edition, W. B. Saunders Company, Philadelphia, Toronto and London. 1,359 pp. with 590 illustrations. $23.00.

Reviewed by: ANTHONY C. NOTO

This work embodies the noteworthy efforts of two pathologists, a biochemist, a clinical chemist and a chief technologist to compile a myriad of up to date medical laboratory procedures and to present the "why" in terms of current knowledge. This ponderous task required the use of 1,359 pages of small print on light paper, supported by an adequate number of illustrations and a generous, appropriate bibliography.

My book weighed 2,440 grams and a copy of the previous edition 1,490 grams, and reflects the collection of almost twice the number of facts of the first edition. Of necessity, many of the more infrequently done special procedures are superficially portrayed and followed by specific references in the current medical literature.

The tome is organized into four sections, collected appendices and an index which is highly detailed and duly cross referenced. The sections are weighted as follows: I. General Knowledge and Chemical Pathology, 14 chapters, 618 pages; II. Hematology, 11 chapters, 193 pages; III. Microbiology, 9 chapters, 173 pages and Histologic Techniques, 15 chapters, 305 pages.

Section I begins with a chapter on the electron micrographic anatomy of a cell with a detailed account of the chemical composition and physiologic functions of its component parts. The subject is developed in depth beyond the point of requirement of the knowledegable average technologist to satisfy the demands of a pedantic theoretician. The chapter includes a cursory examination of how antibiotics act and briefly alludes to the topics of immuno suppressive drugs, nonchromosomal transfer of drug resistance in bacteria and extrachromosomal drug resistance genes in Staphylococci. Mention of these fields of knowledge might just as well have been omitted, yet they serve as an introduction and are redeemed by the appended bibliography which should requite the stimulated reader's curiosity.

Basic principles of laboratory work are reviewed with notes on important safety measures. The rapidly burgeoning subject of clinical chemistry is entered through a portal of definitions, and a review of physicochemical laws, formulas, and principles of organic and biochemistry. Chapter 4 on Methods of Analysis is very timely and treats modern instrumentation, automated analysis, atomic absorption spectrophotometry, chromatography, electrophoresis, radioactive isotopes and quality control. Urinalysis, test of renal function and other organ systems are appropriately covered. The subjects of inborn errors of metabolism and of endocrine investigation are carefully and studiously outlined.

Section II, Hematology, encompasses current knowledge of the corpuscular and fluid components of blood with chapters on classical hematology, coagulation, hemostasis, immunohematology, blood banking and transfusion practices. Discussion of numerous hematologic clinopathologic entities is encyclopedic but brief.

Section III, Microbiology, is noteworthy for the conciseness and practical approach taken in the identification of micro organisms. There are numerous excellent black and white photographs in the chapters on mycology and parasitology, as elsewhere throughout the book, that should assist the student in morphologic diagnosis.

At a time when instructors of medical technology are deemphasizing the subject of histologic techniques, these Canadian Authors have allotted 211 pages of Section IV to the subject. The matter is presented in very good didactic fashion with excellent coverage of the science and art of producing a meaningful slide. If for this part alone, the book merits inclusion among the reference texts a teaching general medical laboratory should possess.

Cytologic diagnosis of section IV has been allotted 32 pages and the final chapter, Cytogenetics, 61 pages accompanied by a comprehensive bibliography of 209 references.

This book should be included in every general medical laboratory's library for its broad, encyclopedic and concise coverage of a vast and ever-growing specialized body of knowledge. It is written clearly with the incorporation of many helpful illustrations, tables, photographs and charts. It is complimentary with some of the longer established works in this field and differs most conspicuously in its elaboration and treatment of the subject of histologic techniques.

THE MYOCARDIUM IN HYPERFUNCTION, HYPERTROPHY AND HEART FAILURE. American Heart Association Monograph #26. Edited by Felix Z. Meerson, M.D. American Heart Association, Inc., New York, 1969. 163 pp. $4.00.

Reviewed by: LOUIS H. NAHUM

This book summarizes the authors important contributions to our understanding of myocardial metabolism, physiology and patho-physiology. The book was translated from Russian into English in Israel under the auspices of the National Library of Medicine. It is based on 10,000 animal experiments.

In the first five chapters the author considers the processes of excitation, contractile function, energy metabolism, nucleic acid and protein synthesis and structural changes developing in the myocardium in compensatory hyperfunction, hypertrophy and heart failure.

In the sixth chapter the role of neuroendocrine mechanisms in the development of hyperfunction, hypertrophy and heart failure is considered. In the last chapter the mechanisms of the processes outlined are used as a basis for experiments on the therapy of acute heart failure and the development of an approach in the treatment of this state in man. Likewise he proposes a method for treating acute myocardial infarction because here also there is hyperfunction in the non-injured regions of the heart.

The experimental therapy employed is to give B_{12} because in this stage of early hyperfunction B_{12} is decreased so also is nucleic acid synthesis. He believes there is an inter-organ transport of resources; thymocytes bring to heart cells precursors and co-factors in nucleic acid synthesis: orotic acid, B_{12} and folic acid. He found that ingestion of folic, orotic acid and B_{12} considerably increased maximum allowable force of the left ventricle.

After trying this method on innumerable animals they studied 80 patients with acute myocardial infarction. Forty were treated with 1½ grams orotic acid, 60 mg. folic acid and 100 micrograms B_{12} daily for two months. Ten of the 40 patients in the control group died, but only 3 in the treated group and none from heart failure. The conclusion for this study is that in addition to generally accepted types of treatment some patients with acute myocardial infarction can be saved if they receive precursors of nucleic acid and cofactors of protein synthesis.

The question, of course, arises first whether the sample is equivalent and whether there were enough cases to warrant the conclusion. The other question is by what method the claimed benefit came about. In animals they found that the concentration of epinephrine in heart muscle falls if no cofactors are given but with treatment this decrease is prevented. Accordingly the author believes that a decreased inotropic influence of the sympathetic nervous system may play a role in the disturbance of the contractile function of the heart.

We would still like to know whether giving isuprel would do the same thing. Nevertheless it is an intriguing theory that Meerson presents and a method of treating acute and chronic heart failure which will now be tried on a greater scale.

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INFANT CARDIAC DISEASE: H. C. Stansel, Jr., M.D. *Guest Editor*

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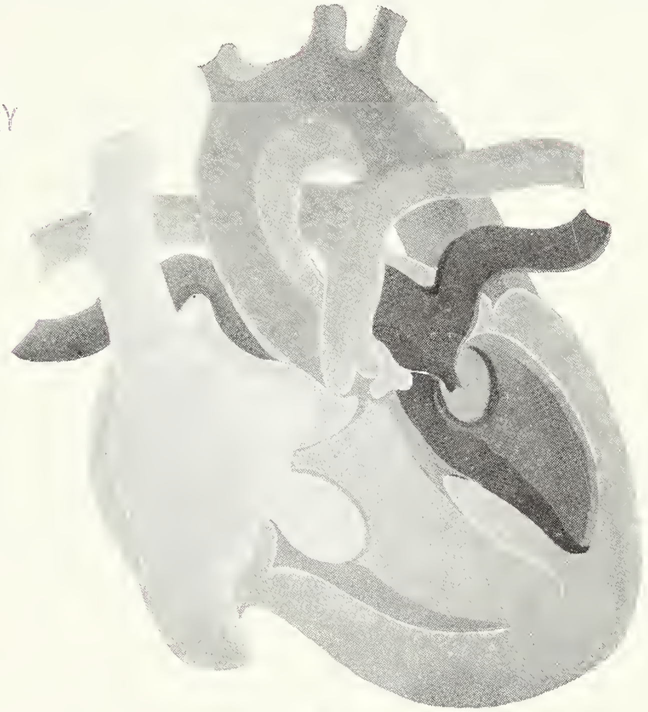

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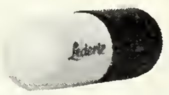

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CONTENTS

editorials

New Approaches To Fertility Control 461
Methadone: Rehabilitation Without A Cure 462
Norepinephrine Turnover In Brain After Administration Of Imipramine: Enhancement By Thyroid Hormone . . . 465
Growing Ones Own Heart Valves 466
The Widening Spectrum Of Therapeutic Uses Of Interferon . 468
A Physiologic Approach To The Treatment Of Essential Hypertension 468
Renal Calculi 470
Electrocardiography And The Family Physician 472
Reflections On Continuing Medical Education 474
The Patient Is Also A Person 478

scientific

Foreword, *H. C. Stansel, Jr., M.D.* Guest Editor 480
The Newborn Intensive Care Unit For Infants With Heart Disease, *A. G. M. Campbell, M.B., M.R.C.P., D.C.H.* . . 481
Recognition And Diagnosis Of The Infant With Critical Congenital Heart Disease, *Norman S. Talner, M.D.* 486
The Radiological Diagnosis Of Congenital Heart Disease In Infancy, *Gerald Fishbone, M.D.* 490
Anesthesiology And The Newborn For Cardiac Surgery, *James I. Gilman, M.D.* 496
Cardiac Surgery In Infancy, *H. C. Stansel, Jr., M.D.* 500

departments

The President's Page 504
From The Executive Director's Office 505
Physician's Placement Service 508
Woman's Auxiliary 527

miscellaneous

In Memoriam 511
Anesthesiology Grand Rounds, *Romulo L. Villar, M.D., Jakub Goldstein, M.D., Samuel M. Lerner, M.D.* and *Frederick W. Hehre, M.D.* 512
Special Article
  Auditing of Physicians' Records, *Arnold J. Streich, L.L.B.* 515
X-Ray Of The Month, *Arnold B. Rilance, M.D.* 518
Electrocardiogram Of The Month, *Hyman N. Chernoff, M.D.* 520
New Books In Review 522
Law-Medicine Notes, *J. Alfred Fabro, M.D.* 523
Letter-To-The Editor 526
Around The State 528
Connecticut Regional Medical Program 529
Connecticut Physicians' Art Exhibition 531
Science News 532

Connecticut Medicine

editorials

New Approaches To Fertility Control

The development of better and simpler contraceptive methods is a part of the general problem of population control. A decade ago birth control technology leaped forward with the development of the oral steroid pill and the plastic intrauterine device (IUD). These were important advances but not ideal. Today the search continues, and both basic and applied research in the fields of reproductive biology are receiving increasing support from the federal government and leading foundations.

The ideal contraceptive is one that would be effective, safe, inexpensive, reversible, easy to use, and acceptable to a diversity of people and cultural groups. This ideal is far from being attained. The problems involved in the use of the pill and the IUD have been widely publicized even though the woman who takes a pill takes far less risk than one who undergoes pregnancy and childbirth, or who has an abortion. In spite of this fact there has been considerable official and unofficial resistance to the use of oral contraceptives in the family-planning program of India and other countries. The IUD has been officially promoted in Taiwan, South Korea, India, and Pakistan, but many women who accepted it initially no longer use it because of side effects which are annoying if not dangerous.[1]

Much is known about the complicated series of events leading to reproduction, but there are great gaps in our knowledge in many areas and "the unknowns loom larger than the knowns". Biologists are not yet sure how the IUD achieves its contraceptive effect. The understanding of the process with which the oral steroid pill interferes, is still far from complete. The pill presently in use upsets the entire hormonal system in addition to stopping ovulation.

Research in reproductive biology should seek to identify ways to achieve contraception without drastic intervention in other bodily processes. The female reproductive system includes an "upper" hormone feedback circuit, consisting of the central nervous system, pituitary and the ovary controlling a "lower" system involving the Fallopian tubes, uterus, and cervix. Most of the research activity has been directed toward understanding the "upper" hormone feedback circuit. Since interference with natural processes at the "lower" level represents a less drastic intervention in bodily function, it is not surprising that new methods of fertility control are directed towards this lower system.

The "pill" affects the higher circuit and is theoretically less desirable than, for example, a method which selectively affects one or more lower circuit links without significant systemic effects. One such experiment was with the "minipill" which provides small doses of progestogen daily. The conventional pill contains both progestogen and estrogen analogs. The minipill does not inhibit ovulation in most cases, but it is somewhat less effective than the conventional pill. The safety of the minipill, however, is not established since beagles on which it was tried began to develop breast tumors.

Another short term approach includes efforts to perfect easier and better methods of sterilization, such as a way to inhibit sperm function by administering low doses of steriods to the male. Another way is to increase the effectiveness of the rhythm method by developing a simple and accurate way to predict time of ovulation. Another way is to improve the IUD.

Long-term approaches to contraceptive development are those looking to new methods that require much more fundamental research before development can proceed. The "once-a-month" pill or injection to be used by a woman to induce menstruation is attractive to family planning specialists in that women would have their menstrual cycle follow a more regular schedule. The Center for Population Research (CPR) is supporting research on prostaglandin compounds which produce degeneration of the corpus luteum in animals. In man, corpus luteum is essential to maintain early pregnancy. These compounds may ultimately offer something approaching an ideal means of fertility control.

Another long-term approach to contraception regarded as promising is through research on "releasing-factor inhibitors." These are the hormones produced by the hypothalamus that control secretion of anterior pituitary hormones, that are responsible for ovulation and development of corpus luteum. The Salk Foundation has been awarded a 2.3 million dollar contract for research on the chemical structure of the gonadotropin-releasing factor. It will then be possible to fashion inhibitors which will prevent pregnancy, or disrupt early pregnancy. Sooner or later we may expect an institute for population research within the NIH that might form a partnership with pharmaceutical companies to promote research on population control.

We must, of course, remember that much could be done to improve family planning and to lower the birth rate if more people were more strongly motivated to use existing contraceptive technology. Since it is easier to change technology than motivation, we must press harder for major new advances in this still underdeveloped field of biomedical research to achieve an ideal method of contraception that would be acceptable to most women.

L.H.N.

Reference

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Methadone: Rehabilitation Without A Cure

Until methadone was introduced to treat heroin addicts their rehabilitation was generally discouraging. Methadone is a synthetic analgesic which offers the most solid promise of practical help for large numbers of heroin users. The treatment involves the substitution of one form of narcotic addiction for another. When administered regularly, methadone blocks the euphoric "high" associated with heroin use. From the experience in New York City impressive results can be expected: addicts have stopped using heroin, have taken regular jobs, or have returned to school, and have broken the pattern of antisocial behavior characteristic of so many addicts.

At present methadone is classed as an investigative drug for long-term treatment of addicts and can be used legally only in federally approved research programs. However, the desperate plight of heroin users has pressured many individual physicians into prescribing for large numbers of addicts without careful supervision or real effort at following research protocols.

The participant in the methadone "Maintenance" program receives a daily dose of the drug for an indefinite period. It is rightly assumed that if methadone is stopped, the person will start using heroin again. Methadone, therefore, offers rehabilitation without a cure. Methadone is now legally approved and used fairly widely for two purposes: as a pain-killing analgesic and to detoxify and withdraw heroin from addicts. The drug is readily obtained by physicians who use it for approved purposes. The point is that long-term treatment programs legally constitute a "new use" for the drug and this is why the FDA has to consider it for safety and efficacy before it is approved for broad use.

Methadone, however, is a narcotic, and this requires setting terms under which it is to be used in addict-treatment programs. When obtained legally, the cost of a daily dose of methadone per patient is very small. However, the total cost of an effective methadone treatment program runs between 1500 and 2000 dollars per year. This is much more than what it would cost if a physician would be able to prescribe it for the individual patient. This simple way, however, has its complexities too because addicts are difficult patients whose prognosis is unpromising.

The New York program established by Dr. Vincent P. Dole at the Rockefeller University in 1963 provides an initial physical examination and treatment for addicts who are usually in poor health. They also receive job and education advice, supportive counseling from staff members, some of whom are themselves former heroin addicts. Two key requirements for accepting patients are that they volunteer for the program and that they do not use drugs besides heroin in significant quantities. Methadone is administered in an oral form, and after patients have reached a stabilized dose level, they are given prescriptions for methadone in pill form. They are required to visit the clinic periodically for a urinalysis check.

The New York program defines success primarily as bringing the patient to the point where he is off heroin and living a free life, free of crime and other antisocial activities. The records show that the program has been successful for 82 per cent of all people accepted. Many of them are leading socially productive lives and are holding jobs or have returned to school.

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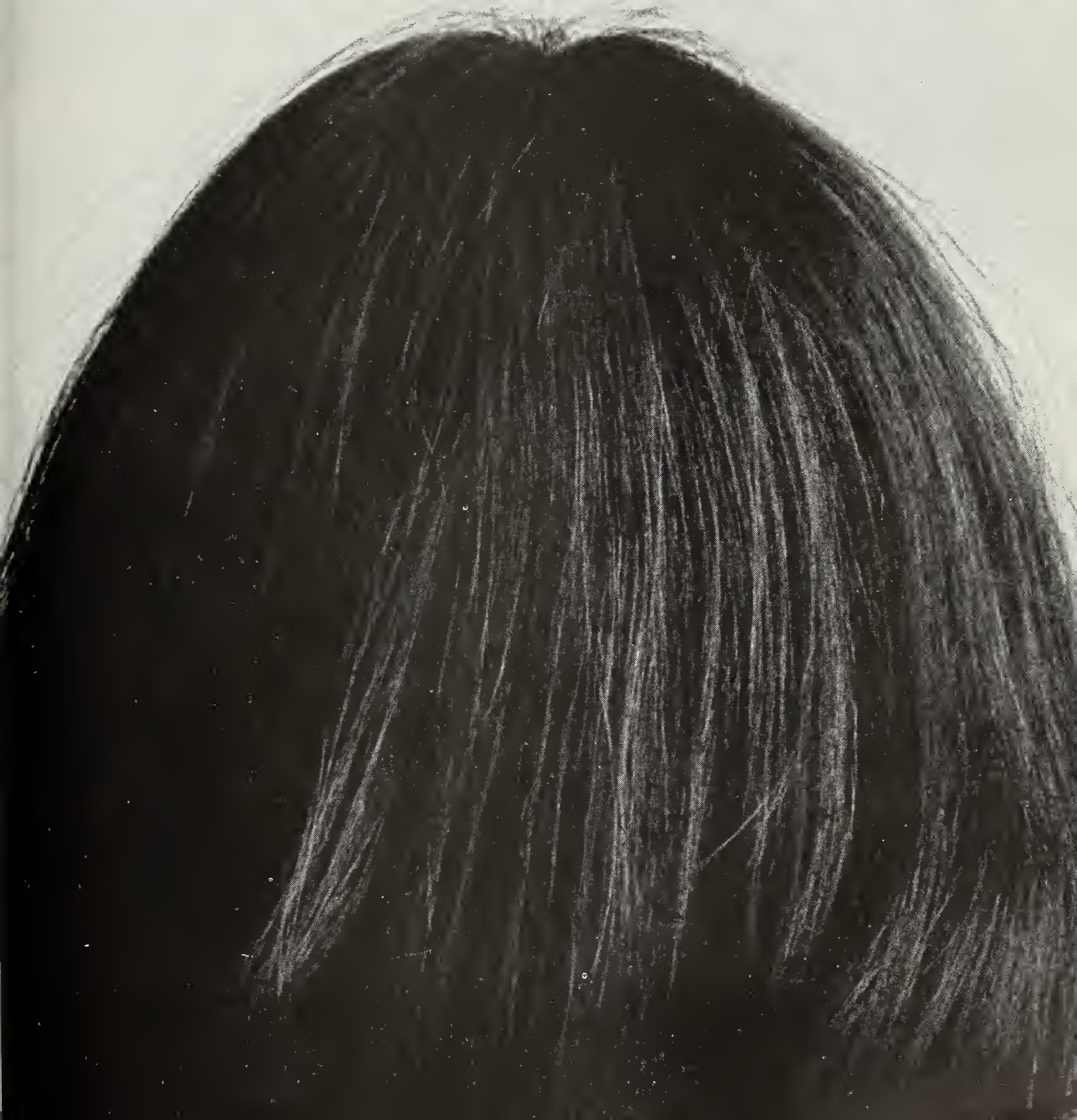
I adore this house.
My in-laws are great.
The neighbors are wonderful.



Indications For use in management of anxiety and tension occurring alone or as accompanying symptom complex to medical and surgical disorders and procedures. Though not a hypnotic, fosters normal sleep through antianxiety and related muscle-relaxant properties

Contraindications. History of sensitivity to meprobamate

Important Precautions. Carefully supervise dose and amounts prescribed, especially for patients prone to overdose themselves. Excessive prolonged use has been reported to result in dependence or habituation in susceptible persons, as alcoholics, ex-addicts, and other severe psychoneurotics After prolonged excessive dosage, reduce dosage gradually to avoid possibly severe withdrawal reactions Abrupt discontinuance of excessive doses has sometimes resulted in epileptiform seizures.

Warn patients of possible reduced alcohol tolerance, with resultant slowing of reaction time and impairment of judgment and coordination.

Reduce dose if drowsiness, ataxia or visual disturbance occurs; if persistent, patients should not operate vehicles or dangerous machinery

Side Effects include drowsiness, usually transient, if persistent and associated with ataxia, usually responds to dose reduction; occasionally concomitant CNS stimulants (amphetamine, mephentermine sulfate) are desirable. Allergic or idiosyncratic reactions are rare, but such reactions, sometimes severe, can develop in patients receiving only 1 to 4 doses who have had no previous contact with meprobamate Previous history of allergy may or may not be related to incidence of reactions. Mild reactions are characterized by itchy urticarial or erythematous maculopapular rash, generalized or confined to groin. Acute nonthrombocytopenic purpura with cutaneous petechiae, ecchymoses, peripheral edema and fever have been reported. One fatal case of bullous dermatitis following intermittent use of meprobamate with prednisolone has been reported. If allergic reaction occurs, meprobamate should be stopped and not reinstituted Severe reactions, observed very rarely, include angioneurotic edema, bronchial spasms, fever, fainting spells, hypotensive crises (1 fatal case), anaphylaxis, stomatitis and proctitis (1 case) and hyperthermia Treat symptomatically as with epinephrine, antihistamine and possibly hydrocortisone. Aplastic anemia (1 fatal case), thrombocytopenic purpura, agranulocytosis and hemolytic anemia have occurred rarely, almost always in presence of known toxic agents. A few cases of leukopenia, usually transient, have been reported on continuous administration

Meprobamate may sometimes precipitate grand mal attacks in patients susceptible to both grand and petit mal. Extremely large doses can produce rhythmic fast activity in the cortical pattern. Impairment of accommodation and visual acuity has been reported rarely. After excessive dosage for weeks or months, withdraw gradually (1 or 2 weeks) to avoid recurrence of pretreatment symptoms (insomnia, severe anxiety, anorexia). Abrupt discontinuance of excessive doses has sometimes resulted in vomiting, ataxia, tremors, muscle twitching and epileptiform seizures. Prescribe very cautiously and in small amounts for patients with suicidal tendencies Suicidal attempts have resulted in coma, shock, vasomotor and respiratory collapse and anuria. Excessive doses have resulted in prompt sleep, reduction of blood pressure, pulse and respiratory rates to basal levels; and occasionally hyperventilation. Treat with immediate gastric lavage and appropriate symptomatic therapy. (CNS stimulants and pressor amines as indicated). Doses above 2400 mg./day are not recommended.

Composition. Tablets, 200 mg and 400 mg meprobamate. Coated Tablets, WYSEALS* EQUANIL (meprobamate) 400 mg (All tablets also available in REDIPAK* [strip pack], Wyeth.) Continuous-Release Capsules, EQUANIL L-A (meprobamate) 400 mg.

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if I don't get away!

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There is another side of the story which comes from critics of the methadone treatment. Methadone does not work satisfactorily for persons who use other drugs besides heroin and who may, in fact, simply add methadone to the mix. Some methadone addicts with expensive habits have learned to use methadone to detoxify themselves in order to reduce their tolerance to heroin so that they may resume heroin at a low dosage. Furthermore, if methadone is made more readily available, heroin users who are not truly addicted, particularly the very young, may be given treatment and make methadone addicts out of them.

The traditional enforcement view represented by the Bureau of Narcotics and Dangerous Drugs (BNDD) is to try and discourage the idea that methadone is a cure for heroin addiction, and is obviously fighting to limit the prescription of drugs to those involved in treatment programs, presumably with controls similar to those in the New York program. They are opposed to giving increased power to the physician to prescribe methadone for fear of misuse of this power. The FDA's position on methadone treatment is that so far, safety and effectiveness have not been demonstrated for the new use of the drug. Methadone is apparently to be continued in its present status as an investigational new drug (IND), that is, it can be used only in approved programs that meet departmental criteria for research on humans.

It is difficult to reconcile the existing food and drug laws and narcotic laws, recognizing the possibility that soon thousands upon thousands of persons may be under long-term treatment with a drug that is not officially classed as safe and effective. How will the federal authorities meet this dilemma? It will require regulations governing the medical aspects of the use of methadone and regulations governing the security and diversion written by BNDD in the Department of Justice. Such regulations and the manner in which they are enforced will be of particular interest as a test of whether or not there is to be a significant change in the treatment and rehabilitation of narcotics addicts.

L.H.N.

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Norepinephrine Turnover In Brain After Administration Of Imipramine: Enhancement By Thyroid Hormone

A relative deficiency of norepinephrine or other biogenic amines at critical receptors in the brain may occur in some depressive disorders. It has been suggested that the changes in biogenic amine metabolism produced by antidepressant drugs may account for their clinical effects. It is known that Imipramine and various other tricyclic antidepressants inhibit the uptake of norepinephrine and alter the turnover and metabolism of this amine in the brain.

A single dose of imipramine inhibited the uptake of norepinephrine but the content of endogenous epinephrine of the brain was not altered.[1] After long term administration of imipramine, the uptake of norepinephrine into brain was inhibited as evidenced by lower concentrations of norepinephrine. However, the concentrations of metabolites of norepinephrine, normetanephrine increased.

On the basis of data from studies on depressed patients treated with imipramine, it has been suggested that this drug may decrease norepinephrine biosynthesis. This cannot be determined from Schildkraut's present data.

Small doses of thyroid hormone when combined with imipramine seem to produce more rapid clinical improvement in depressed patients than does imipramine alone.[2] Thyroid hormone may also accelerate the development of the changes in turnover and content of norepinephrine in brain which are produced by long-term administration of imipramine. Norepinephrine disappeared from brain more rapidly and the content of endogenous norepinephrine in brain was lower after 10 days of treatment with imipramine in combination with a relatively small nontoxic dose of thyroxine than after 10 days of treatment with imipramine alone.

In depressed patients long-term administration of imipramine facilitates the restoration of normal functioning in spite of relatively reduced concentrations of endogenous norepinephrine, by increasing its availability at receptor sites.

These findings suggest that in addition to thyroxine, other hormones and pharmacological agents or physiological and behavioral techniques which increase the turnover of norepinephrine in brain when administered with tricyclic antidepressant drugs, may also accelerate and enhance the clinical antidepressant effects of these drugs.

L.H.N.

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Growing Ones Own Heart Valves

Doctor A. G. Geha presented a report on growing ones own heart valves in Washington, D.C., at a meeting of the American Association for Thoracic Surgery. Others have used valves made from other autogenous tissues such as arteries, the pericardium, and fascia lata. It is, however, very difficult to make exact copies of the valve cusps from flat sheets of tissue. A technique of producing autogenous valves would, therefore, be of great help. It is true that prosthetic valves are easier to make, but their use is complicated by a high incidence of thromboembolism. Preserved aortic valve homografts and heterografts do not lead to complications, but do not survive long because of late deterioration and failure. Fresh, viable homografts "take" well, but are no answer to the problem because the supply is so limited.

Dr. Geha and his associates perceived the idea of growing the heart valves in the patient himself. He observed the fibrocollagenous tissue complex that forms around silastic pacemakers and other implants. He had seen Dr. R. T. Padula using it successfully for the replacement of both superior and inferior venae cavae in dogs. Accordingly, Dr. Geha made their molds by pouring silastic into aortic and pulmonary roots taken from sacrificed dogs. Each root mold was then divided into three cusp molds along the lines of the deep clefts in the area of cusp apposition.

The first part of the study involved planting ten such molds of different sizes and shapes under the panniculus carnosus of the abdominal wall in each of 20 adult mongrel dogs. Physical and histologic studies of the molds and surrounding tissues at various intervals showed that the fibrocollagenous tissue matures in about 12 weeks. The fibrocollagenous membrane so formed was easy to separate from the adjacent areolar tissue. The material held sutures well, was easy to work with, and proved strong enough to withstand high aortic pressures.

The next step was to use the molded autografts for valve replacement in living dogs. The investigators implanted several individual cusp molds in each of 12 adult mongrel dogs and removed the fibrocollagenous membrane after it had reached maturity. The membranes were then used to replace a single semilunar cusp in each of 25 adult mongrel dogs. Some received autografts and others homografts.

The replacement of the right coronary cusp or noncoronary aortic cusp was associated with a high mortality and all died in 24 hours. Examination of the implated valve, however, showed them to be competent in all dogs. The cause of death was not related to aortic valve function. During their lives the dogs maintained good diastolic pressures and normal pulse contours. Some of the dogs became hypertensive as a result of the drugs they received, but the valves functioned well and showed no damage or tear. Neither did the valves induce any inflammatory response in the host tissue.

Valve replacement surgery was more successful in 5 other dogs who each received a semilunar pulmonary autograft. All dogs survived the postoperative period and 2 continued to do well 5 weeks later. Hemodynamic studies from 24 hours up to 5 weeks after operation showed no pressure gradient across the valve and a normal pulse contour in the pulmonary artery. Angiograms at various intervals also showed the valve remained competent.

One of the dogs who received an autograft was sacrificed 4 weeks after operation and showed solid fibrous union between the graft and the host. The original fibrocollagenous graft tissue appeared still viable. The pulmonary artery aspect of the replaced cusp was smooth and glistening. The ventricular aspect was smooth and dull.

Two dogs who had received homografts were sacrificed 3 to 4 weeks after operation. The replaced cusps were surrounded by a deposit of fibrin and platelet thrombus. Histological examination showed no remaining viable graft tissue. What this means is that one can't depend on graft valves from another person, but that in the future a patient with aortic valve disease will have to grow his own valve replacements before surgery, then they will remain viable when successfully implanted.

L.H.N.

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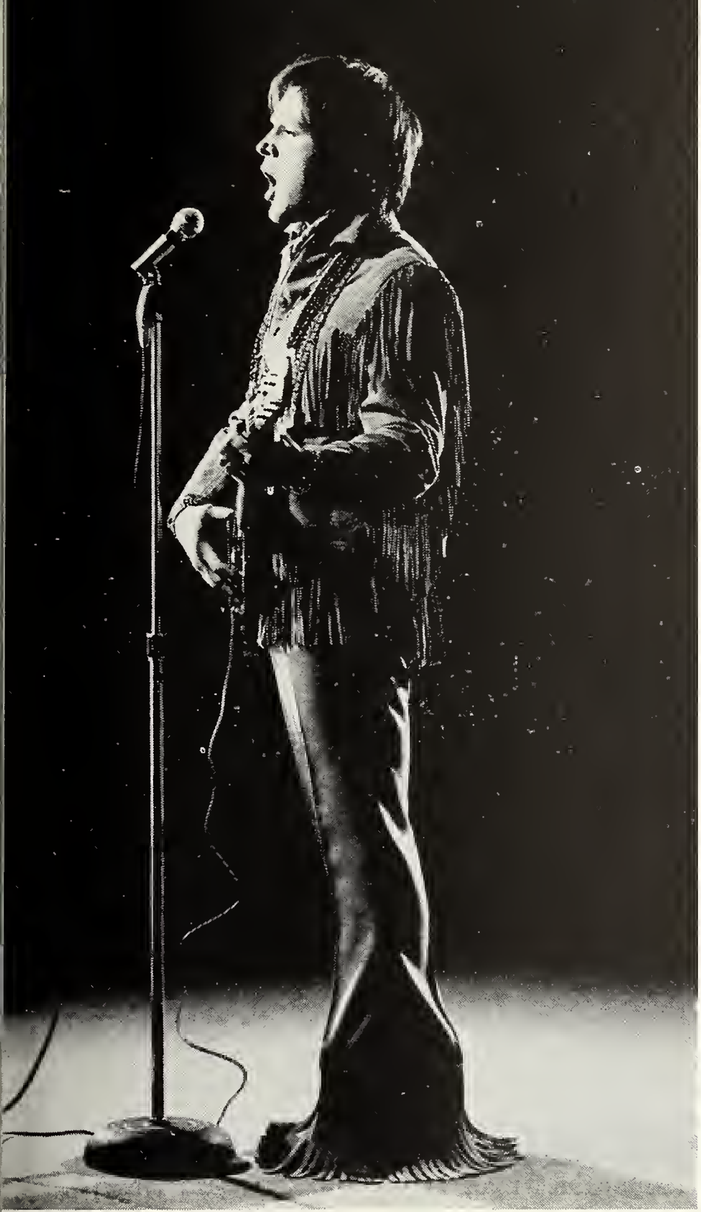

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The Widening Spectrum Of Therapeutic Uses Of Interferon

Research in interferon has come a long way since its beginning twelve years ago. When Isaacs and Lindenmann first detected interferon, they hoped modestly that their findings would help explain the mechanism of viral interference. Much of the interest in this cell-derived protein since then has stemmed from the appreciation that interferon is a widespectrum and nontoxic antiviral agent. More recently, interest in interferon has been heightened by the finding that a number of species of double-stranded ribonucleic acids can stimulate cells to produce interferon. A powerful tool has thus become available for the study of interferon production and action. It has also brought us closer to possible new approaches to the practical therapeutic uses of interferon.

A recent symposium on interferon was held in New York City, December 5-6, 1969 under the auspices of the New York Heart Association which reflected the great interest in interferon inducers. One paper reported on interferon production in chick embryo cells which superficially resembles induced enzyme synthesis in bacteria. Both double stranded RNA as well as single stranded can also serve as the inducer molecule. Yamazaki reported producing a quite purified—albeit probably still not quite pure—from rabbit cell interferon with a stunning specific activity of 4.8 × 10^7 units per mg. of protein. The way this interferon works is by a selective suppression of viral protein synthesis by the cell.

The role of interferon in the pathogenesis of viral infections and the relationships of interferon and other specific immune reactions were the subjects of papers by S. Baron and L. A. Glasgow. They pointed out that recent developments have suggested that interferon and specific immunity are not fully independent. In particular, it has become clear that lymphocytes not only play an important role in the production of antibody and in the cell-mediated types of immune response, but they are also an important source of interferon. Moreover, as demonstrated by Glasgow, immune lymphocytes respond to a homologus viral stimulation with increased interferon production.

The final part of the symposium was devoted to two recently recognized activities of interferon—the inhibitory effect on human growth and the suppression of intracellular multiplication of some protozoal parasites. H. B. Levy from the N.I.H. discussed his findings on the suppression of the growth of various malignant tumors in mice by a double-stranded polynucleotide interferon inducer (poly I- poly C). It is still uncertain whether all this antitumor effect is interferon mediated.

The involvement of interferon seems likely, however, in view of I. Gresser's independent demonstration of the suppression of mouse tumor growth by the passive administration of interferon. Since both interferon and poly I-poly C exert an inhibitory effect on tumors not known to be of viral origin, this activity cannot be the result of the antiviral action of these agents. Similar problems are posed by the already demonstrated effect of interferon and of several interferon inducers against mouse malaria (R. I. Jahiel, N.Y.U.). These findings indicate that interferon can no longer be considered a strictly antiviral agent.

It is obvious that research on interferon has advanced rapidly in only a decade. Although our understanding of the mechanisms of interferon production and action has remained quite rudimentary, nevertheless these recent developments suggest that the clinical application of this research may soon be forthcoming. The spectrum of application is widening so that it may come to be used not only as an antiviral agent but also against malaria and finally against some cancers.

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L.H.N.

A Physiologic Approach To The Treatment Of Essential Hypertension

The basic fault in essential hyptension is widespread peripheral vascular constriction.[1] This is generally associated with a normal or at times low cardiac output. The logical approach to therapy should be to remove the constrictive "clamp" on the arterioles by active vasodilation. The problem here is that if vasodilatation effectively brings down the arterial pressure, a greater venous return should occur and with this increased cardiac output and cardiac acceleration will also occur. The ideal treatment, therefore, would seem to be one that produces peripheral vasodilation and at the same time reduces the reflex cardiac response to it.

The number of direct vaso-dilators available clinically are quite few. Organic nitrates lead to tolerance and are, therefore, employed in the treatment of acute hypertensive crises. Diazoxide is also restricted in use to acute therapy because it also produces hyperglycemia. The only generally valuable vasodilator in the chronic treatment of hypertension is hydralazine. This drug, however, has only limited power in patients with hypertension. Accordingly, it is necessary to add to hydralazine, hexamethonium or guanethidine or alphamethyl-dopa to inhibit adrenergic nervous function.

This produces the desired reduction of peripheral vascular resistance, but also decreased cardiac output, interruption of vascular reflexes with postural hypotension and a variety of minor symptoms that derive from interruption of total adrenergic function. These side effects become particularly prominent in patients with severe disease in whom almost total inhibition of adrenergic function may be required to control arterial pressure. It seems that a more powerful vaso-dilator than hydralazine when combined with selective inhibition of only the cardiac adrenergic nervous function should provide better antihypertensive action with fewer side effects.

Laboratory studies have indicated that a piperdine-pyrimidine derivative (PDP) is a powerful vasodilator that directly relaxes smooth muscle with no impairment of adrenergic function. Gilmore[2] now reports his results on 11 hypertensive patients with PDP to achieve active vasodilatation of the arterioles and propranolol to produce selective cardiac adrenergic inhibition. Their experience in this small number of essential hypertensives indicate that PDP is a powerful antihypertensive drug and when combined with propranolol in appropriate dosage provides effective control of arterial hypertension.

PDP has a marked antihypertensive effect consistently observed in all patients. It does not produce postural hypotension. It does not reduce glomerular filtration rate or effective renal flow. It does, however, lead to increased venous return which produces moderate tachycardia and increased cardiac output. This increased cardiac activity is undesirable because more oxygen is needed by the heart muscle and, therefore, it might precipitate myocardial ischemia. In fact, there were several patients with ECG change suggesting ischemia. Such reflexly induced alterations in cardiac activity has been treated with ganglionic-blocking drugs, but with undesirable side effects as noted above.

However, if one uses propranolol it is selective in inhibiting only cardiac adrenergic receptors. Heretofore, its use has not been widely adopted except in certain patients with spontaneous excessive cardiac activity. Gilmore's experience with PDP and propranolol, however, is that the heart rate and cardiac output increase resulting from peripheral vaso-dilation was attenuated and heart performance remained unaffected. If we knew whether augmented adrenergic activity subsided as PDP therapy was continued, then there might be a reduction in the need for propranolol. This remains to be seen. It appears as though sodium retention which occurred with all Gilmore's patients on PDP is also a property of other vasodilator drugs such as hydralazine and diazoxide and can readily be corrected by a diuretic such as hydrochlorothiazide.

There were other untoward effects of PDP during its short-term clinical administration which were confined to the cardiovascular system. There were minimal T-wave changes. This could have been due to myocardial ischemia induced by increased cardiac activity in patients with occult coronary heart disease. There is, of course, the possibility that perhaps PDP produces a myocardial abnormality directly. Further clinical evaluation will be required to determine the persistence of the antihypertensive effect and the frequency and type of toxicity during long-term administration of the drug.

At this moment it seems likely that the combination of a powerful vasodilator PDP acting directly on the arterioles, together with beta-adrenergic blockade of the heart sympathetics by propranolol may provide more effective control of hypertension with fewer side effects than currently available drugs that inhibit the total adrenergic function.

L.H.N.

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Renal Calculi

Yent[1] studied 439 patients with renal calculi at the Toronto General Hospital for a 13 year period. Almost half of the patients were suffering from Idiopathic hypercalcemia which was rarely due to hyperparathyroidism. In this latter instance the author stresses the importance of detecting minimal degrees of hypercalcemia both from serum calcium levels and shortened QT interval in the electrocardiagram. Only 5 percent were due to hyperuricemia and 2 percent of the stones were due to cystinuria.

Having identified the nature of the stone by chemical analysis one then searches for an underlying metabolic disorder which directs our attention to prevention of future stones. Prevention of uric acid stones is easily accomplished by forcing fluids and perhaps alkalinizing the urine which might in fact occasionally dissolve a present stone. However, in the presence of infection or gout, allopurinal is much the best method.

In cystinuria both water and alkali have to be used aggressively. The urinary output must be brought up to 3 liters per day and urinary pH to 8 or better. Then if such patients don't respond but continue to form cystine stones 5 d-penicillamine is the drug of choice. It combines with cystine to form a soluble disulphide which results in marked lowering of cystine excretion. This method can also dramatically dissolve cystine stones. The trouble is that d-pencillamine is expensive and has some toxic effects in some patients.

With calcium stones it's another matter. High fluid intake is still important, especially in the evening to obtain dilute urine during the night. Osler and others have suggested the use of distilled water. There appears to be some property in hard waters that contributes to stones. On the other hand there are islands in the West Indies where the population suffers a very low incidence of stones and the natives' entire water supply is that of distilled water.

Restricting dietary calcium is frought with too many failures. Some restrict milk and milk products, but this is unsatisfactory because such a diet results in a decrease of orthophosphate intake now being used with a fair degree of success. Since 65 per cent of all kidney stones contain calcium oxalate which occurs regardless of urinary pH, restricting oxalate containing foods

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might help; such foods as spinach, asparagus, rhubarb as well as tea, coffee and chocolate.

Many other methods have been tried and abandoned except for inorganic phosphates. In doses of 3-4 grams per day this chemical is quite effective in preventing calcium oxalate stones. However, it requires a goodly dose, with the side effects such as diarrhea. Furthermore, it is not good in triple phosphate stones associated with urinary tract infection.

Another approach to the problem of recurrent calcium stones involves the use of thiazide 50-100 mg hydrochlorothiazide per day. These cause a marked reduction in urinary calcium excretion in practically all kinds of patients including hyperparathyroidism. The thiazides lead to a positive calcium balance and increased urinary magnesium. To avoid potassium loss one can add aldactone to the thiazide.

The question is frequently asked what happens to the calcium which was formerly excreted in the urine, where is it going. Dr. Yent found no evidence of calcification in soft tissues. After an initial phase of thiazide administration, which may be months in duration, the calcium which is not being excreted in the urine is simply not being absorbed by the gut. However, thiazides do have a definite effect on the skeleton. Careful studies led Yent to conclude that thiazides diminish bone absorption at least for awhile. Accordingly, it would be interesting to know whether it is a good agent also in osteoporosis.

Thiazides were not synthesized until 1956 and have been used as a diuretic and anti-hypertensive agent. Their value in preventing kidney calcium stones is only indirectly related to their diuretic effect. So far no other diuretics have been found to affect calcium and magnesium metabolism in this fashion. Hippocrates advised fluids and diuretics in treatment of kidney stones. This is the method today except that our diuretics are potent and his were not.

L.H.N.

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Electrocardiography And The Family Physician

The diagnosis of coronary artery disease is often one of the most difficult problems which the family physician faces and as a rule an electrocardiogram is essential. This is especially true in patients with many "risks" factor and in view of the fact that among these silent infarcts are not rare. The question arises who should record an electrocardiogram and how should it be reported.

Three answers have been suggested. The first is that every patient with suspected coronary disease should be referred to a cardiologist. Although a cardiologist seeing such a patient would lead to the most accurate diagnosis, there are obvious disadvantages. First is that it would overload the cardiologist with an overly great increase in the volume of his work. Another objection would be that of delay. Unless special arrangements were made for this type of consultation, the patient would often have to wait several days if not longer for an appointment. Another disadvantage of this scheme is the loss of clinical independence of the family doctor. It would clearly be an advantage if he could manage the situation by himself without referring the patient to another physician.

A second suggestion is that the family doctor should have his own electrocardiograph and thus be self-sufficient. This would overcome the disadvantages of the first scheme. Delay would be reduced to a minimum and he would be self-supporting. The disadvantage of this method is the question of the accuracy of the diagnosis. Only those with experience in this field appreciate the difficulty of accurate diagnosis of coronary artery disease. The electrocardiogram is far from being a magic box. It is certainly not a doctor.

One of the major problems is that when an infarct is small and recent, an electrocardiogram may show no abnormality. Another is that it may show evidence of infarction in a patient whose symptoms are non-coronary, for instance a patient with pleurisy cervical spondylitis or cholelithiasis, who has had a silent infarct in the past. It is often impossible to tell from a single tracing whether the abnormality is old or recent. Another difficulty is a differentiation between left ventricular hypertrophy and lateral wall infarct.

Very few family physicians have either the training or the experience to enable them to make an accurate assessment of coronary artery disease by the electrocardiogram in their patients. A crash course in electrocardiographic re-

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porting would help, but it is not the ultimate solution, because apart from the recognition of the common arrhythmias, electrocardiographic interpretation cannot be learned quickly. In any case there is so much more to coronary artery diagnosis than just interpretation of the electrocardiogram. The doctor to undertake the work would be one who has been trained for a long time in a cardiac department and who undertook the diagnosis of coronary artery disease after such qualified training.

The third suggestion is a private or hospital based electrocardiogram reporting service. There have been several encouraging reports of its use one by Magana et al.[1] This scheme has the advantage of an expert opinion on the tracing while leaving the family doctor in control of the clinical situation. Its drawback lies in the fact that the electrocardiogram so rarely shows clear evidence of infarction and so often shows only slight non specific abnormalities. Coronary artery disease can be diagnosed accurately only if the ECG and the clinical picture in all its detail are synthesized by one experienced doctor. Detailed knowledge of the patient's systems, the shape of his chest, the character of the apex beat, the presence and quality of heart sound murmurs as well as the level of blood pressure, the drugs the patient is taking, all are essential in diagnosis.

The physician requires an unequivocal answer to the question, does the patient suffer from coronary artery disease and if so, is it progressive. Long experience of an electrocardiogram reporting service has led cardiologists[2] to conclude that a cardiologist with a single ECG and a brief note before him can seldom give it. The minor variations on this scheme by which the family physician records the electrocardiogram and sends it to the cardiologist for reporting has the advantage of speed, but against this is the disadvantage that the tracing can be less reliable than that recorded by an expert technician either in a hospital or private consulting service.

The answer to the problem of coronary artery disease in general practice is an emergency consultation service, either in a hospital or private electrocardiographic service. The disadvantage of the emergency services in a hospital is that the physician overseeing such patients may not himself be an experienced electro cardiographer.

L.H.N.

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Reflections On Continuing Medical Education

The concept of a lifetime of learning has become an accepted fact of life for those in the health professions. The knowledge explosion which challenges undergraduate medical education has an even greater impact on the practicing physician. Regional medical programs have made available millions of dollars to close the information gap between the research bench and the patient's bedside. The AMA is now involved in the formal accreditation of continuing medical education programs. The literature contains many reports of the reactions of participants (what they did or did not like). A few investigators have focused on the testing of achievement, but studies attempting to relate the quality of medical care in terms of its outcome, to the continuing education of physicians are rare.

Youmans[1] in 1935 came to several conclusions, among them, the fact that practical work or working with patients under supervision, was the most valuable learning experience. He also believed that the teacher in postgraduate education should possess not only knowledge, but a sympathetic appreciation of the problems and limitations of busy practice.

The next study came from Peterson[2] in 1954 about physicians in North Carolina. This was primarily an inquiry into the quality of medical care. He could find no evidence of an association between the quality of care and participation in continuing education programs. On the other hand Roney and Roark[3] found that physicians participating in continuing education at the University of Kansas were more competent than those who did not. Those attending did more complete physical examinations including ophthalmoscopy and more pelvic examinations. They ordered fewer laboratory procedures but more Papanicolaou tests.

Lewis's[4] study focused only upon participation of Kansas physicians in continuing education offered at the University. It made no at-

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tempt to categorize and quantify the involvement of physicians in formal postgraduate education outside the state, at local medical meetings or to ascertain their personal reading habits. Lewis did not demonstrate an association between involvement in continuing medical education and certain end-results, measures of medical care over a ten year period in perinatal and maternal mortality. Apparently there are other factors, inadequate techniques of teaching and learning and perhaps socioeconomic factors that are more important determinants than the fact for participation in continuing education.

Medicine is not the only field that is suffering from the impact of the knowledge explosion. The short half-life of new information in medicine and other fields such as engineering requires the development of methods for preventing professional obsolescence. Medicine lacks organizational structures to assume responsibility for directing the continuing education and retraining of physicians. With the exception of large group practices that can make such arrangements for their members, physicians must individually schedule their own time off, define their own needs and voluntarily cease income-producing activities to keep abreast of current developments. This seems to be a heavy responsibility for the individual physician.

The current pattern of organization in medical practice as well as the work load carried by busy physicians, seems to make formal periodic retraining difficult. A recent study by the California Medical Association[5] indicated that approximately 50 per cent of all hours of continuing medical education in that state was provided by the medical schools. Only seven per cent of physicians took most of the course work. It may be assumed these doctors were conscious of their own needs as well as those of their patients and were motivated to practice high quality medical care.

Participation in continuing education apparently depends upon inculcating in the physician a sense of responsibility for self-education and continued retraining. At present there are few external forces to require involvement, let alone learning, in such programs. However, the need for continual retraining must increase as knowledge grows. If the present methods are ineffective, then those concerned with continuing medical education should be aware of the danger of merely doing what it has been doing thus far.

Miller[6] has commented on the shortcomings of current methods now employed rather extensively in postgraduate education. These have been described as passive learning, content-oriented or categorical. The question is posed whether content-oriented education can mount successful process-oriented continuing education programs. To increase the effectiveness of continuing medical education several changes seem necessary. In the first place, methods employed in continuing medical education must involve the physician actively in learning in areas where he has been made aware of his deficiencies.

Programs must help physicians to identify their needs recognized and unrecognized. There must also be a method of stimulating those who will not voluntarily engage in such activities. The Board of Family Practice has a provision for relicensing every six years upon evidence of participation in active learning programs. The argument in favor of this has been presented by Stein.[5]

It may turn out that some reorganization of the pattern of medical practice may be the solution to the problem of relieving the physician of the burden of his day to day practice and financial costs associated with retraining. Large group practices do have the means to allow the members continuing education. Organizations other than Universities may eventually have to share the enormous responsibilities of supporting programs necessary for a life time of learning. The Connecticut Regional Medical Program is pointing the way in offering $500 to the physician for the two weeks he takes off from his practice to become proficient in a coronary care unit.

L.H.N.

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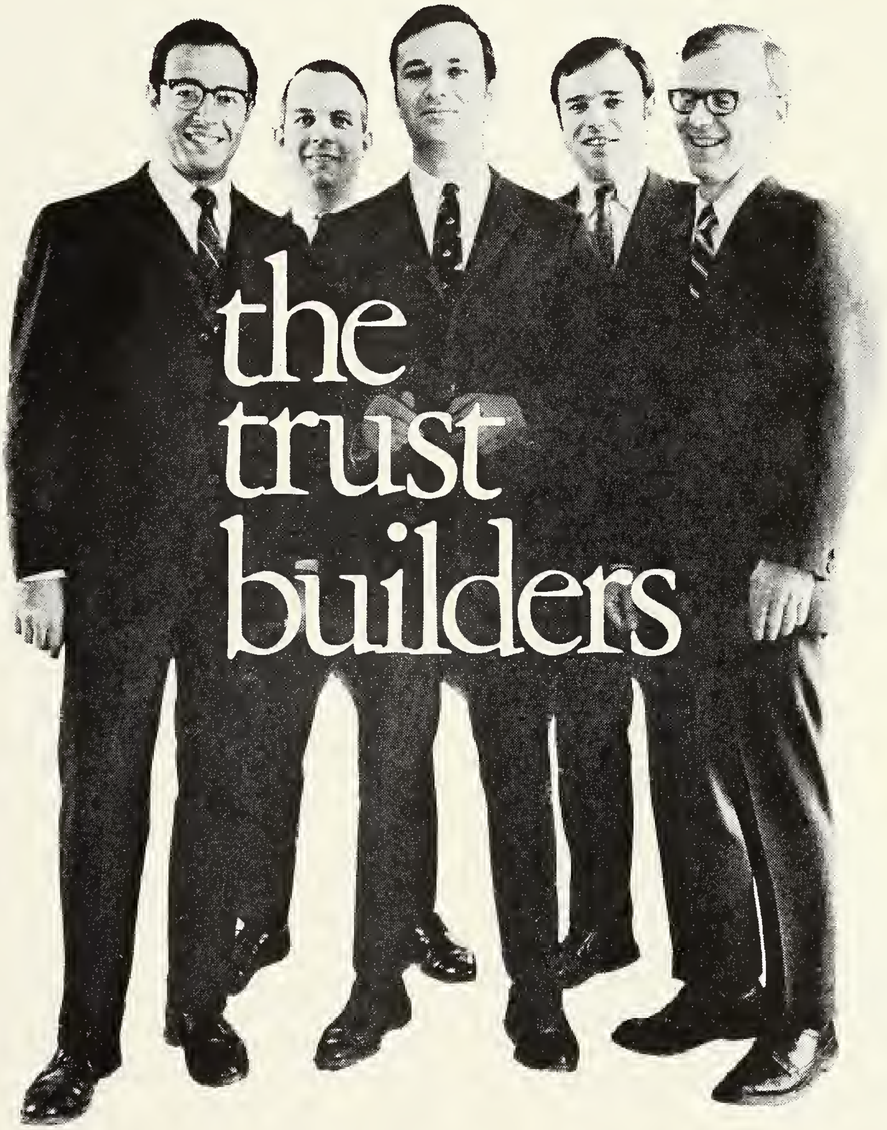

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The Patient Is Also A Person

An understanding of the psychosocial aspects of physical illness is one of the most important contributions that behavioral sciences can make to medicine. It is generally acknowledged that the total management of a patient requires knowledge of the psychological and social aspects as well as the physical aspects of a patient's illness. In fact psychosocial stresses alone can be a causative factor in human diseases and this is an important area for investigation. The psychiatric consultation services in the general hospitals during the last 2 decades have given some students of human behavior an opportunity to study reactions to somatic disease, hospitalization, to diagnostic, and therapeutic procedures and much more.[1]

The psychiatrists have had to try to understand how the patient experiences his illness regardless of its cause, how he copes or fails to cope with it, how the family interaction is affected by and in turn affects the sick member, how the patient-doctor relationship evolves and gives rise to conflicts and a host of other pertinent issues. A conceptualization is needed in this whole area which is equally relevant to medical practice as well as to the study of human behavior.

If we view disease from a purely biological angle, it is an abstract concept devoid of psychological and social connotation. The medical dictionary, however, gives us a broader concept, "the sum total of the reactions physical and mental, made by a person to a noxious agent entering his body from without or arising from within". In this definition disease is viewed as a state having no separate existence from a patient—a person. A person is more than a biological organism for it encompasses a realm of feeling and of symbolic activities of thought and language. Furthermore, a person is also a member of a social group with which he interacts. In short a concept of disease is not complete unless it takes cognizance of these facts.

How a person experiences the pathological process, what it means to him, and how this meaning infiuences his behavior, his interaction with others are all integral components of disease viewed as a total human experience. What a person experiences is directly known only to him. We can learn about it by obtaining his introspective reports. We can perceive behavior both verbal and non-verbal and describe them, make references about unobservable psychic processes. Here we need to make a clear distinction between a description of a phychosocial phenomenon and the explanations we attribute to the phychological processes which determine them.

To explain why a person responds psychologically to a given disease process or injury it is necessary to consider first of all the patient's personality and relevant aspects of his life history. We need to know the patient's current social and economic situation. We should have some information of the patient's non-human environment. Finally, we should understand the nature and characteristics of the pathological processes, injury or physical disability as they are perceived and evaluated by the patient. In short the resulting psychological response includes the intrapsychic (experiential), the behavioral and the interpersonal or social. These factors refer to what the patient perceives, what he feels, and what he thinks. What are his actions, his communications, and his interactions with others, especially his family and the doctor.

To understand how the patient experiences his illness and how he copes with it, we need to know what all aspects of his disease mean to him. We all know how some individuals react with alarm to harmless palpitations or any other bodily perception which is new to him. If he anticipates some danger whether realistic or not, it is often accompanied by anxiety and anxiety has some physiological concomitants such as tachycardia, hyperventilation, which themselves also produce further symptoms and enhancement of anxiety.

Anxiety now sets up cognitive functions aimed at avoidance, minimization or warding off of the anticipated danger. In this way the unpleasant experience of anxiety is eliminated. Lipowski explains the numerous strategies used by individuals to reduce anxiety arising from some threat such as unconsciously operating defense mechanisms such as denial of danger all the way from compulsive overwork or sexual activity to the intake of sedatives or alcohol.

How does a person react to loss, either bodily parts, functions actually lost and to deprivation of personally significant needs and values? Any decrease may involve partial or total deprivation of sources of pleasure and self-esteem. Then such losses lead also to disturbed interpersonal relationships which result in further actual or feared loss. The emotional response to real or anticipated loss takes the form of a grief reaction. This at times may assume a psychopathologic form such as a depressive syndrome, self-destructive behavior, hostility, paranoid reaction or even elation.

Sometimes disease results in relief of a sense of guilt especially if the disease means deserved punishment to the patient or satisfaction of dependent needs. Sometimes patients will use one's illness to arouse guilt in others so that they can control others and ensure compliance with their wishes. They are helped to avoid social stresses and achieve abatement of inner conflicts. The patient may be entirely unaware of his unconscious pressures. On the whole where subjective gains derived from illness and disability outweigh the losses, then the patient is likely to cling to his sickness and develop an emotional disturbance when recovery occurs. An example is physiological improvement after surgery but psychological disorder.

Lipowski warns that whenever an illness has lasted for a long time, there is a possibility that the patient may have derived from it gains that could not be removed with impunity. Then a thorough psychological evaluation before radical intervention in such cases is mandatory.

In short to understand how the patient experiences his illness and copes with it one has to know what all aspects of his disease mean to him and what responses to his complaints he obtains from other persons and his doctor. What threat does the patient experience, what loss does he perceive, what gain is he deriving from his illness.

Psychosocial factors do influence the course and outcome of illness and it is imperative that their evaluation should be a fact of medical diagnosis and management.

L.H.N.

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Foreword

NEW HOPE FOR THE INFANT CARDIAC

This special edition of Connecticut Medicine attempts to provide the reader with the latest developments in the diagnosis and management of cardiac disease in the infant.

The clinical recognition of cardiac pathology during the first weeks of life depends upon a high degree of suspicion. Tachypnea and cyanosis in the newborn is all too frequently attributed to amniotic fluid aspiration or other noncardiac pathology. Close cooperation between the pediatric cardiologist and the radiologist is necessary if these infants are to be recognized. Once the clinical diagnosis of symptomatic cardiac disease is entertained cardiac catheterization is indicated before one can proceed on an intelligent basis. If one waits until the infant is critically ill, the risks of the catheterization itself becomes significant. At this point the chances of the child surviving palliative cardiac surgery diminish greatly. There is now sufficient experience to enable one to predict which lesion will permit the child to survive with or without medical or surgical intervention. This judgement, however, can only be made after the diagnosis is confirmed by cardiac catheterization and angiocardiography.

If these infants are to survive cardiac surgery skilled anesthetic management and rapid precise surgical techniques are mandatory. Intensive post-operative care guided by careful monitoring is equally important if acceptable survival rates are to be achieved.

In summary, we have presented in this seminar an approach to the management of the infant with cardiac disease. These small people present difficult problems requiring highly specialized techniques and close cooperation between pediatric cardiologist, radiologist, and pediatric cardiac surgeon. Rigid adherence to the principles described here, however, have been proven to provide hope for most all infants born with cardiac disease.

H. C. Stansel, Jr. M.D. *Guest Editor*

The Newborn Intensive Care Unit For Infants With Heart Disease

A. G. M. Campbell, M.B., M.R.C.P., D.C.H.

The Newborn Intensive Care Unit For Infants With Heart Disease

Special care nurseries for premature and sick newborn infants have become accepted in many countries throughout the world as a vital part of concerted efforts to reduce neonatal mortality and morbidity. During the past few years a number of major medical centers, including the Yale-New Haven Medical Center, have established large intensive care nurseries for infants with all the major problems of the newborn period. The facilities available in these nurseries are particularly appropriate for an infant with a serious heart defect.

Newborn Intensive Care

To provide intensive care for the newborn, it is essential to develop an organization of concerned and interested persons, trained in newborn observation and care, who can be present or immediately available twenty-four hours a day. A large amount of sophisticated equipment for monitoring and therapy is valuable, but it should be stressed that a high standard of intensive care can be achieved with very little equipment. Conversely, unlimited equipment will not compensate for deficiencies in personnel.

The Newborn Special Care Unit— Yale-New Haven Hospital

This unit in its present form was largely made possible through the generosity of Eleanor Naylor Dana and was opened in May 1967. The Director at that time was Dr. Louis Gluck. The nursery incorporates several innovative features in design and in policy. It provides space for 37 infants in four main nurseries but over 40 infants can be accommodated if necessary. One of the four main nursery areas is shown (Fig. 1).

An important and relatively recent trend in

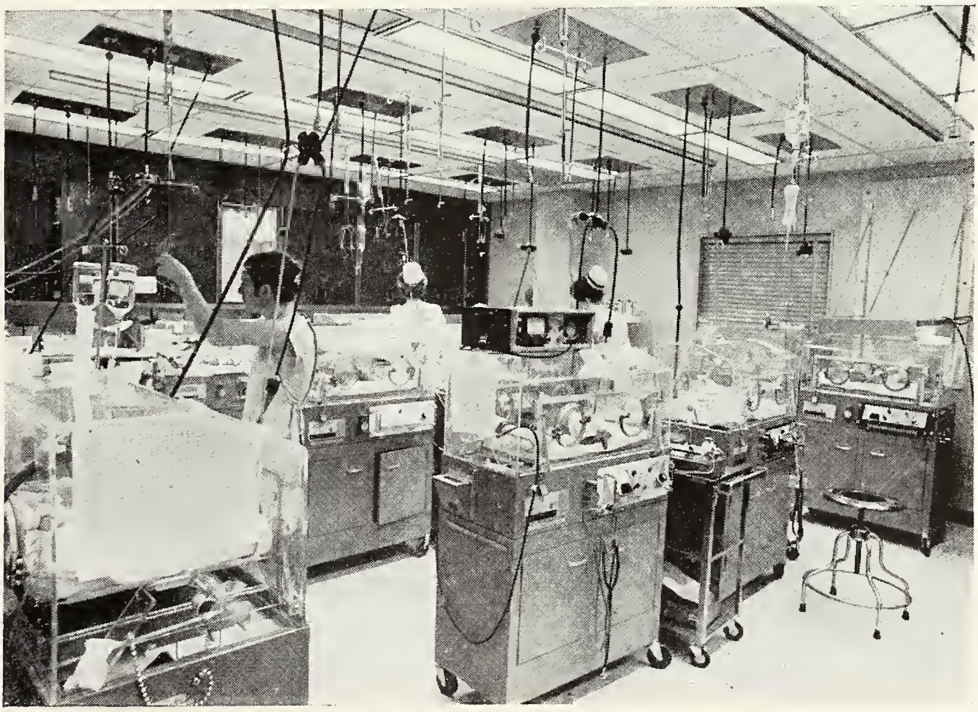

Figure 1

Maximum care nursery with ceiling outlets for oxygen, air, suction and electric power.

DR. A. G. M. CAMPBELL, Associate Professor of Pediatrics, Yale University School of Medicine; Director Newborn Service, Yale-New Haven Hospital, New Haven, Conn.

nursery practice that has been adopted is the concentration in one maximum care area of all infants on admission, irrespective of their diagnosis or origin, until their individual needs can be fully assessed. This includes for example, infants who are premature or mature; infants who have heart disease, intestinal obstruction or meningitis; infants born in our hospital, admitted from the emergency room, born at home or referred from another hopital. The principal stipulation made is that they should need the facilities for observation, consultation and treatment that the unit can provide and that by being in the unit they can receive the best care. The most important factor in achieving maximum intensive care is a high standard of nursing and medical observation, anticipation and reaction to emergencies. The concentration of infants in large open areas ensures good observation for all and avoids the nursing of infants in separate rooms or cubicles, isolated and far removed from adequate supervision. To date there has not been any major problem of cross-infection. Recent research and clinical experience in newborn nurseries seem to indicate that isolation can best be achieved by hexachlorophene bathing of infants and rigorous attention to the cleaning of hands and equipment before making contact with each baby.[1, 2] However, individual isolation for contagious infections is also possible within the intensive care unit.

Although the majority of infants admitted to the unit is derived from the Yale-New Haven Hospital obstetric service this includes healthy premature infants and infants admitted for short periods of observation and treatment. During the past few years there has been continuing development of the newborn special care unit as a regional service. With the exception of the hospitals within the city of Hartford, almost every other hospital in Connecticut uses the unit for the referral of infants with special problems such as respiratory distress, surgical emergencies and congenital heart disease. These infants admitted from the region are almost all very sick and require maximum intensive care.

Infants With Congenital Heart Disease

Recently, the development of the New England Infant Cardiac Program has led to a more coordinated attempt to improve the identification of infants with serious congenital heart disease and to expedite their rapid transportation to referral centers in New England.[3] For some years the Yale-New Haven Hospital has been the major referral center for Connecticut and in volume of referrals is second in New England only to the Children's Hospital Medical Center in Boston. Each year about 700-800 infants are admitted to the unit. About one quarter of these are seriously ill infants referred to the center for further diagnosis and treatment from the region and a significant number are infants suspected of having congenital heart disease. (Table 1) A newborn special care unit is ideally suited for the intensive observation, evaluation and care of a sick infant with heart disease both before and after any cardiac surgery that may be indicated. Some of the ways in which the personnel and facilities of such a unit can contribute to the care of the infant with heart disease will be discussed.

Communication

A newborn special care unit is operational 24 hours a day, seven days a week and can be reached at any time. Some similar units have established a "hot line" telephone for this purpose. With the recently introduced "Centrex" telephone system, referring physicians can reach the resident in charge of the unit directly at any hour and arrange for an infant's admission. (Telephone number: [203] 436-8940) Further consultation on arrival can then be arranged with a Pediatric Cardiologist who also is available on call 24 hours a day for urgent consultation and initiation of investigation and treatment.

Transportation

Connecticut is in a relatively fortunate position with regard to the transportation of patients from one hospital to another. It is small and compact and an ambulance journey is not likely to exceed two hours in any direction within the state. It is favored by a network of good roads which are rarely impassable even in the worst winter conditions. However, there are some communities which lack ambulance facilities adequate for the particular needs of sick newborn infants. Infants with heart disease may

TABLE 1

OCTOBER 1, 1969-MARCH 31, 1970

Source of referral	*Total*	*Number with C. H. D.*	%
Yale-New Haven Hospital	287	8	2.8
Connecticut	88	24	27.3
New York State	2	1	—
Massachusetts	3	1	—
Totals	380	34	8.9

Admissions to the newborn intensive care unit over a six-month period. Note the significant number of infants admitted from community hospitals with the diagnosis of congenital heart disease.

require oxygen, airway maintenance and the correction of acidosis, all requiring the constant attention of skilled personnel. Finding suitable facilities may considerably delay referral thus increasing the risk of death before diagnosis and treatment. In the near future a central ambulance transportation service will hopefully be developed which will cater to these special needs of sick infants. At the request of the referring physician and with the co-operation of local ambulance companies, an ambulance will be dispatched to the community hospital. A special transport incubator to provide warmth, oxygen and humidity is available from the intensive care unit and in certain circumstances a physician or nurse will accompany the ambulance. Intensive care procedures such as umbilical artery catheterization and the correction of acidosis can then be performed in the community hospital. In this way the infant can be prepared for transfer and maintained in optimal condition for further evaluation.

Observation and monitoring

A newborn intensive care unit is particularly suited for the close observation of sick infants and this would include the great majority of infants referred with congenital heart disease. These infants will usually present with cyanosis, tachypnea or heart failure, may deteriorate quickly and little time can be spent in reaching a diagnosis if surgical palliation or correction is to be offered.

The nurses and physicians must be familiar with the importance and significance of such features as cyanosis, tachypnea and abnormal heart rhythms and rates. In particular, if they are experienced in the problems of the newborn, they will be aware of how rapidly the clinical picture can change. The major readjustments in the circulation that normally take place at birth can be influenced by such frequent complications of birth as inadequate ventilation, hypoxia and acidosis to the extent that adaptation may be prolonged. Against this background of unstable hemodynamics the recognition of major abnormalities of the heart and their differentiation from primary lung problems can be very difficult. Sudden variations to arterial hypoxia or hyperoxia, the onset of apnea and cardiac slowing are all situations that may require urgent and appropriate action.

Complementing and supplementing the intelligent observation of experienced nurses are various types of monitoring equipment to record and alert personnel to such potentially dangerous complications as episodes of apnea and alterations of heart rate and rhythm. In any situation of cardio-respiratory difficulty it has become standard practice in newborn intensive care units to monitor both the oxygen concentration of the infant's environment in the incubator and the arterial pH and blood gases. The maintenance of blood gases and pH (especially PO_2) within relatively narrow limits is essential if optimum management is to be achieved. Not only can too little oxygen be harmful to newborn infants but too much oxygen must also be avoided to minimize the risk of pulmonary or retinal oxygen toxicity.

The interpretation of the blood gases and pH can be of considerable diagnostic value in the evaluation of the infant suspected of having heart disease.[4] This test may be helpful in avoiding cardiac catheterization in an infant with delayed adaptation, it may be valuable in determining the optimal time for surgery and it is useful in following post-operative progress.

Evaluation and Treatment

An infant with congenital heart disease who becomes symptomatic during the first few days of life can deteriorate very rapidly from hypoxemia and acidosis or congestive heart failure and the facilities for diagnosis should be such that rapid clinical evaluation can be followed by cardiac catheterization and appropriate treatment, medical or surgical, in a matter of hours. A newborn intensive care unit is ideally suited to such a purpose. We have learned the value of early identification of congenital heart disease so that the great majority of infants presenting with congenital heart disease in this age group can at least have the diagnosis confirmed or made by cardiac catheterization and angiocardiography. In this way no infant, even if critically ill, is denied the possibility of palliative or corrective surgery for lack of a precise diagnosis.

If this program of evaluation and treatment is to proceed smoothly a team approach is essential with cooperation and communication between the newborn service, the pediatric cardiologists and the cardiovascular surgeons.

Clinical assessment. As an infant is admitted he is assessed by history and examination. An X-ray of chest and electrocardiogram are usually obtained within an hour of admission. During this time, depending on age, umbilical artery catheterization or radial artery puncture will be performed (procedures with which the staff of newborn intensive care units should be fully familiar) and an arterial blood sample obtained for pH, PO_2, PCO_2 and base deficit. This can be determined within minutes in an adjacent laboratory and with micro-sampling techniques so that blood loss is minimal. It must be stressed that umbilical artery catheterization is a technique which should be reserved for sick infants when monitoring of blood indices is essential for evaluation and care. There is significant risk of sepsis, thrombosis and embolus formation particularly when the catheter is left in situ for long periods e.g. over forty-eight hours.

In addition to the clinical examination and the X-ray and E.K.G., the interpretation of these pH and blood gas changes while breathing air and oxygen can be very valuable in demonstrating any functional derangement of hemodynamics, especially in the differentiation of congenital heart disease from some other (usually pulmonary) cause of respiratory difficulty and cyanosis. An appreciation of the acid/base status of such a sick newborn infant and if necessary appropriate correction can be vital if cardiac catheterization is to be performed at minimal risk. An outline of the important steps that have become routine for full assessment of an infant who is suspected to have congenital heart disease is shown. (Table 2)

Radiology. In addition to routine roentgenograms, special magnification films of the chest can be obtained in the radiology diagnostic suite situated within the intensive care unit. These films have proved helpful in interpreting some of the patterns of abnormal lung vascularity seen in congenital heart disease and in differentiating these from abnormalities of lung parenchyma.

TABLE 2

1. *History:*
    Age of Onset, Presenting Features Etc.
2. *Clinical Assessment:*
    Size and Gestation Age
    Color
    Respiratory Pattern; Tachypnea
        Hyperpnea
    Pulses and B.P.
    Heart Sounds
    Murmurs (Bruits Over Other Sites?)
    Hepatomegaly
    Associated Anomalies
3. *Electrocardiogram*
4. *Chest X-Ray:*
    Heart Size, Shape and Pulmonary Vascularity
5. *Arterial pH and Blood Gases:*
    In Air and Maximum O_2
6. *Cardiac Catheterization and Angiocardiography*

An outline of the major steps and clues in the evaluation of a newborn infant who presents with symptoms and signs suggestive of congenital heart disease.

Cardiac catheterization. A decision on cardiac catheterization can be made within an hour or two of the infant's admission and during this time various therapeutic measures such as digitalization and the use of diuretics can be instituted as indicated. Any hypothermia that has occurred during transfer can also be corrected. In extremely sick or moribund infants an angiographic study adequate for diagnostic purposes can sometimes be made through the umbilical artery catheter in the aorta. Frequently this will already have been inserted in the newborn nursery for monitoring purposes. Special transport incubators are available to convey the infant to the cardiac catheterization laboratory. These incubators and other heating units which can be used during cardiac catheterization are invaluable in controlling the infant's body temperature and in maintaining him in optimal condition. The cardiovascular surgeons are notified of infants proceeding to catheterization and are often present in the catheterization laboratory during the procedure. This ensures that, in the event of a diagnosis such as pulmonary atresia with severe hypoxemia or coarctation of the aorta with congestive heart failure, palliative or corrective surgery can be performed immediately.

Occasionally it may be harmful to a very sick infant to transfer him some distance to the cardiac catheterization laboratory. The diagnostic radiology suite within the intensive care unit will shortly be equipped so that urgent cardiovascular studies can be done within the newborn intensive care area.

Post-operative care. After cardiac surgery and a temporary period of immediate post-operative stabilization the infants are returned to the newborn intensive care unit. Here, continuous monitoring of such parameters as ambient oxygen concentration, arterial pH and blood gases, and respiratory and heart rates can be continued. The other assets of such a unit for newborn infants such as the skilled newborn nursing and the use of special feeding techniques and diagnostic procedures are then available until the infant is ready for discharge. Should assisted ventilation be required in the post-operative period then this too can be continued. A volume respirator (Bourns) specially suited for newborn infants is part of the basic equipment of the unit. Other types of monitoring equipment are constantly being added. For example a mixing valve to vary the oxygen concentration delivered to a respirator or isolette and a complete monitoring station for heart and respiratory rates, blood pressure and E.K.G. are now available.

Continuity of care. The newborn intensive care unit involvement in the pre-operative and post-operative care of infants with congenital heart disease means that this very important aspect of care can be maintained. This is particularly reassuring for the parents of a very sick infant. The birth of a baby is normally a happy event but when a serious abnormality is suspected or detected in the baby the distress and shock to the parents is particularly severe. In the newborn intensive care unit particular efforts are made to maintain very close contact with the parents by such means as involving them with some of the practical aspects of care so that they can have a clear understanding of the problem and realistically plan for the infant's care at the time of discharge. Numerous changes in nursing and medical personnel are often inevitable but if, as far as possible, the infant is nursed in one area for most of his stay in hospital, much confusion and loss of contact between hospital staff and parents can be avoided.

Social work service. A most important additional service available in the newborn intensive care unit is given by the full-time social worker. She can be of enormous help and comfort to parents about a wide variety of problems while the baby is in the hospital and can aid them in preparation for the infant's return home. By the nature of their illness, a fairly large proportion of the infants in a newborn special care unit have created major social and economic difficulties for their families. A considerable part of the social worker's time is devoted to helping the parents of infants with congenital heart disease.

Teaching and Research

Two other very important functions of such an intensive care unit which should be considered in any discussion of its role are teaching and research. A central intensive care unit for the region provides an ideal opportunity for demonstrating to community physicians and health personnel as well as to medical students, house staff and post-graduate fellows all of the important aspects of the evaluation and care of critically ill newborn infants. With over 50 infants with congenital heart disease admitted each year there is ample opportunity for developing considerable experience in a wide range of conditions.

In the same way the intensive care unit provides an opportunity for various studies in clinical research such as the evaluation of new techniques and new methods of treatment. These aspects are essential to the maintenance and improvement of high standards of patient care.

How far newborn special care units have been successful is difficult to determine. The individual nurseries vary widely in such considerations as the definition of intensive care, the type of population served, admission policies, and the availability of personnel and equipment. Because of these variations statistics are difficult to obtain and even more difficult to evaluate. In addition, major changes and improvements in infant care have occurred regardless of the setting. However, at a recent conference on the problems of neonatal intensive care units there did seem to be some agreement and a certain amount of data to support the impression that these units are accomplishing some reduction in newborn mortality particularly with infants of low birth weight.[5] The full impact of these special nurseries on neonatal morbidity is yet to be assessed.

Thus a newborn intensive care unit with its personnel and equipment is concerned with all infants referred to it who need intensive care. Sharing in these facilities are a significant number of infants who are suspected of having congenital heart disease sufficiently serious to be symptomatic in the neonatal period.

Now that so much can be done for these infants in the way of palliative or even corrective surgery, the early identification, rapid evaluation and skilled nursing care of these infants have become vital factors in achieving total success. It is in these areas that the newborn intensive care unit can play a major role.

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Recognition and Diagnosis of the Infant With Critical Congenital Heart Disease

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Any program designed to increase the salvage of critically-ill infants with congenital heart disease must rest on the foundation of early recognition, safe and rapid transportation to an infant cardiac center, precise diagnosis, and appropriate medical and surgical management. This portion of the symposium will concern itself with the problems related to case finding and diagnosis. It reflects an approach to the infant suspected of having significant cardiac disease which has been developed over the past five years as the Yale Infant Cardiac Consultation Service now incorporated into the New England Regional Infant Cardiac Program.[1] Basic to this approach is the underlying philosophy that no infant is too ill to be evaluated by cardiac catheterization and angiography or to have an emergency surgical procedure which may improve the underlying hemodynamic state. This requires that practicing physicians and nurses in newborn units recognize the possibility of a cardiac problem and to initiate the chain of events which may culminate in the salvage of that particular infant.

Functional Classification of Critical Cardiac Disease in Infancy

As a generalization, the infant with severe cardiac disease suffers from either congestive heart failure or hypoxemia existing singly or in combination. From the functional standpoint, congestive heart failure may arise from a) volume overload of the circulation typified by the large left-to-right shunt, large systemic arteriovenous fistulae, or valvar regurgiatation; b) obstruction to left- or right-ventricular outflow (pressure overload) as in aortic atresia, critical aortic stenosis, severe coarctation, or pulmonary valve stenosis with intact ventricular septum; and c) obstruction to pulmonary venous return as in anomalous pulmonary venous connection either below or above the diaphragm. Hypoxemia results from either obstruction to pulmonary blood flow with right-to-atrial or ventricular shunting or inadequate mixing of the systemic and pulmonary circulations as in transposition of the great arteries. Compromise of ventilatory function arising from pulmonary congestion may also induce hypoxemia.

In volume overloading, diastolic filling of the ventricles is increased and the precordium is usually hyperdynamic. With large volume left-to-right shunts or systemic arteriovenous fistulae, respiratory symptoms dominate the clinical picture due to the increase in pulmonary artery and venous pressures which produce pulmonary congestion. Consequent to the increase in pulmonary pressures and flows, there may be vascular compression of the large bronchi and signs of respiratory obstruction (wheezing) will be evident. Under these conditions, secondary lung infections can occur. Complicating airway problems, of course, make the differential diagnois between primary lung disease and cardiac disease difficult and cardiac catheterization may be necessary to clarify the picture.

Low cardiac output states arising from obstructive lesions involving the left heart characteristically present with signs of impaired peripheral perfusion and are frequently confused with septicemia. Peripheral arterial pulsations under these conditions are diminished, body temperature subnormal, and the skin mottled. Elevation of pulmonary venous pressure secondary to left-heart obstruction will be reflected by respiratory rates in the range of 100 per minute. Right-sided congestive heart failure is manifested by hepatic enlargement and occasionally by peripheral edema and is seen along with pulmonary congestion. In situations such as pulmonary valve stenosis with intact ventricular septum, only signs of systemic venous congestion, including hepatomegaly and rarely peripheral edema, are present.

With pulmonary venous obstruction seen in association with anomalous pulmonary venous connections, respiratory symptoms related to pulmonary venous hypertension will be evident. There is right-sided cardiac failure with hepatic enlargement and hypoxemia arises from atrial right-to-left shunting. Since in these conditions blood is trapped in the pulmonary and systemic circulations, cardiac cham-

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ber size may be normal, although pulmonary edema (coarse reticular-granular pattern) is evident on the chest X-ray.

Cyanosis is the principle finding in lesions associated with obstruction to pulmonary blood flow or limited mixing of the systemic and pulmonary circulations and demands further studies to delineate its etiology. It cannot be emphasized too strongly that cyanotic infants or, for that matter, infants in cardiac failure do not improve unless prompt medical or surgical measures are instituted. Watchful waiting has no place in the approach to either of these situations. In assessing the cyanotic infants, murmurs may or may not be present, while the second heart sound is usually single (even when two semi-lunar valves are present as in transposition of the great arteries).

Role of Fetal Flow Pathways and Pulmonary Vascular Bed in the Expression of Cardiac Disease in the Infant

The persistence of fetal flow pathways and heightened reactivity of the pulmonary vascular bed may be the major determinants of the clinical picture of cardiac disease in the neonate.

Patent ductus arteriosus: In certain conditions (i.e., pulmonary atresia), the ductus arteriosus constitutes the sole blood supply to the pulmonary circulation, while in other situations (aortic atresia) is the only avenue for systemic perfusion. In the latter, when the ductus constricts, systemic blood flow is compromised and signs of inadequate peripheral perfusion ensue. When the ductus is the only source of pulmonary flow (i.e., pulmonary atresia), the level of arterial P_{O_2} constitutes the only reliable measure of adequacy of the pulmonary circulation. If the P_{O_2} is less than 35 mm Hg and if the infant is living off his ductus arteriosus, an intolerable situation exists which demands improvement. If the ductus closes spontaneously, rapid demise may occur, while continued patency with a low P_{O_2} requires attempts at improving pulmonary blood flow. A survey of ductal size in patients with obstruction to pulmonary blood flow revealed that the ductus may be smaller than normal fetal channel (only carrying 5 to 10% of cardiac output rather than the total right ventricular output) and, therefore, limits the extent of pulmonary perfusion.

Foramen ovale: The foramen ovale may allow right-to-left shunting in situations with right-heart obstruction or underdevelopment (tricuspid and pulmonary atresia). As previously mentioned, it is the only access to the left heart in anomalies of pulmonary venous connection. The size of the atrial opening may also be crucial in determining access of systemic venous blood to the left heart and must be taken into consideration in planning medical and surgical management.

Left-to-right atrial shunting takes place through an incompetent foramen ovale in anomalies associated with underdevelopment of the left heart and elevated left atrial pressures as has been observed with large volume left-to-right shunts.

Ductus venosus: This fetal channel closes shortly after birth but could provide a temporary low resistance bypass of the liver in situations with anomalous pulmonary venous connection below the diaphragm. This explains the delay in the onset of symptomatology for one to two weeks which has been observed in these infants.

Pulmonary vascular bed: The highly reactive pulmonary vascular bed in the newborn period is the primary determinant of the clinical picture in patients with shunt lesions. Persistence of a high pulmonary vascular resistance delays the appearance of symptoms in patients with large communications at the ventricular and pulmonary artery level (ventricular septal defect, patient ductus arteriosus, aorticopulmonary window). When pulmonary vascular resistance does fall usually at the end of the first month, pulmonary flow then increases and signs of congestive heart failure (including tachypnea, tachycardia, hepatomegaly) ensue. In high output states associated with arteriovenous fistulae, a high pulmonary vascular resistance may be retained, resulting in right-to-left foraminal and ductal shunting in a clinical setting which in the adult would not be associated with hypoxemia.

Clinical Features of Cardiac Disease in Infancy

It is apparent from the preceding sections that tachypnea and cyanosis are the hallmarks of significant cardiac disease in the infant. Tachypnea, characterized by rapid, shallow respirations (> 60 per minute) unassociated with grunting, is the major sign indicating the presence of congestive heart failure. Once observed, the infant requires further evaluation to detect underlying cardiac disease. Rapid respirations are observed in infants with large left-to-right shunts, left-heart obtruction, and with obstruction to pulmonary venous return and reflect elevation of pulmonary venous pressure.

The cyanotic infant also demands immediate evaluation to assess whether this arises from obstruction to pulmonary blood flow with right-to-left atrial or ventricular shunting or inadequate mixing of the systemic and pulmonary circulations as encountered in transposition of the great arteries.

There are several other clinical features of critical cardiac disease in infancy which also deserve mention. The quality of the peripheral arterial pulsations may afford an index of peripheral perfusion. Decreased arterial pulsations are noted in low output states, while bounding arterial pulsations may be observed in situations where there is an aortic run off, i.e., patent ductus arteriosus or systemic arteriovenous fistula. The latter may produce signs of congestive heart failure in the first few days of life. A discrepancy between the brachial and femoral pulses should always raise the possibility of coarctation of the aorta.

In the newborn period, the presence or absence of murmurs is not as helpful a sign as in the older infant or adult and in many instances, because of the nature of the pulmonary vascular bed, murmurs may be atypical. A careful search should always be made for cranial or hepatic bruits as an indicator of the location of a systemic arteriovenous fistula. The second heart sound should be carefully assessed. The presence of splitting implies that there are two semi-lunar valves, while absence of splitting may raise the possibility of only one.

Hepatomegaly is another frequent finding in the infant with congestive heart failure usually following signs of left-sided involvement (tachypnea). Systolic pulsations of the liver are seen with regurgitation of the tricuspid valve, while presystolic pulsations may be noted when there is obstruction to right atrial emptying. Peripheral edema and ascites are rare findings in association with cardiac failure in infancy and indicate advanced functional impairment.

Laboratory Aids in the Assessment of the Infant with Cardiac Disease

1. *Chest X-ray:* All infants with signs of respiratory distress require chest roentgenograms for proper clinical evaluation. This study will delineate cardiac size, the status of pulmonary perfusion, the presence or absence of pulmonary parenchymal disease and visceral position.

2. *Electrocardiogram:* While the range of normality and abnormality is wide, the finding of marked right ventricular or right atrial enlargement or the absence of right ventricular predominance may be helpful in clinical assessment.

3. *Blood gases and pH:* These determinations while breathing room air and following 100% oxygen administration may aid in the differential diagnosis of pulmonary and cardiac problems. It may also give some information as to the index of systemic perfusion and adequacy of ventilatory function. In our experience, a metabolic acidemia has accompanied low output states (aortic atresia, critical aortic stenosis) and severe hypoxemia (transposition of the great arteries, pulmonary and tricuspid atresia), while respiratory acidosis has been observed with pulmonary venous obstruction and congestive heart failure associated with large volume left-to-right shunts.[2] A striking rise in P_{O_2} (> 20 mm Hg) following the administration of 100% oxygen for seven to 10 minutes argues for pulmonary factors being responsible for hypoxemia but does not completely rule out a cardiac problem.

Cardiac Catheterization and Angiocardiography

All infants referred for cyanosis or congestive heart failure are studied unless blood gas, pH, or roentgenographic assessment indicates that pulmonary parenchymal disease is likely. If in doubt, the patients are studied. In prosecuting these investigations, we feel that the risk to the infant because of his cardiac problem is greater than the risk of the study, although unquestionably the risks in the newborn period are higher than at any other time. While it is difficult to separate procedural mortality from the basic underlying condition, our figures indicate a 1.5 to 2% risk factor for this group during the past few years.

The study is carried out by a group of experienced professional and technical personnel on 24-hour emergency call. During the procedure, temperature is controled with a servo-operated heating unit and blood gases, pH, and arterial pressure are monitored. Ultramicro methods are used for blood sampling (sample size 0.2 cc). Soft catheters are utilized and the study is performed under image intensification in a lighted room. Intubation and defibrillatory equipment are close at hand.

Selective injection of contrast material is carried out as needed during the study and the films reviewed using an instant video replay device so that the study can be completed in a minimal amount of time, usualy less than one hour. Oxygen is administered via a hood unit, if necessary, throughout the procedure. The surgical team is notified when a procedure is starting and is present at the time of the study. This affords prompt transfer to the cardiovascular surgical suite for operative intervention, if this is deemed indicated.

The recent introduction of the technique of balloon atrial septostomy, for situations where there is limited mixing between the two circulations or obstruction at the foramen ovale level, affords the use of the cardiac catheter as a therapeutic as well as a diagnostic tool.[3]

Summary

The approach to the infant with critical congenital heart disease requires early recognition of the signs of congestive heart failure and cyanosis and prompt referral to an infant cardiac center for definitive diagnosis and treatment. Since symptoms present in the newborn period are associated with a potentially lethal situation, the physician must be alerted to the importance of tachypnea and cyanosis in his assessment of infants. If either of these signs is present, a high index of suspicion for cardiac disease must be entertained and further investigations are absolutely necessary. Definitive diagnosis can be accomplished in critically-ill infants, if these studies are carried out under controlled conditions, and a surgical team is available to proceed immediately if the situation so requires. The operation of such a program of prompt recognition, improved diagnosis, and early surgical intervention should result in an increased salvage of these high-risk infants.

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Delicate and difficult as was the task of measuring the pulse in Galen's time, he was clever enough to anticipate by seventeen centuries some of the tests which modern psychologists have urged that should be applied in criminal trials. He detected the fact that a female patient was not ill but in love by the quickening of her pulse when someone came in from the theater and announced he had seen Pylades dance. When she came again the next day Galen had purposely arranged that someone should enter and say that he had seen Morpheus dancing. This and a similar test on the third day produced no perceptible quickening in the woman's pulse, but it bounded again when on the fourth day, Pylades' name was again spoken.—From Lynn Thorndike's History of Magic and Experimental Science (C 1923) Vol 1., p. 144.

The Radiological Diagnosis of Congenital Heart Disease in Infancy

Gerald Fishbone, M.D.

The contribution of the chest X-ray to the diagnosis of congenital heart disease in infancy is quite variable. In some instances, the diagnosis can be made on the basis of the chest film alone, while in others the contribution of the plain film is negligible. There are few times when the radiographic findings are characteristic of a specific anomaly; in most cases, however, the radiologist can narrow the diagnosis down to a few specific possibilities and, by correlating the roentgenographic findings with the clinical features, suggest which of these possibilities is the most likely.

There are many excellent classifications of congenital heart disease based on embryological, anatomical or clinical features. From the radiological point of view, however, the single most important feature in classification is the state of the pulmonary vasculature. On the basis of the appearance of the pulmonary vascularity patients can be placed into one of five broad diagnostic groups. a.) Those with increased pulmonary flow, b.) those with decreased pulmonary flow, c.) those with normal pulmonary flow, d.) those with increased pulmonary vascular resistance, and e.) those with increased pulmonary venous hypertension [Table 1].

Before considering each of these groups separately, a word on evaluating the pulmonary vasculature may be helpful. In evaluating the pulmonary vasculature, particular attention should be given to the appearance of the vessels in the middle and outer third of the lung fields. Normally second, third and fourth order branches are visible in the middle third of the lung. Few vessels are seen in the outer third. One or two end-on vessels are usually seen near the hilum and an occasional one more peripherally. When an end-on artery is seen side by side to an end-on bronchus, both structures have similar diameters.

In patients with increased pulmonary blood flow, the vessels in the middle third of the lung are enlarged. Fourth, fifth and sixth order branches may be identified and followed into the outer third of the lung. The size and number of end-on vessels near the hilum are increased and the arteries appear larger than their accompanying bronchi. [Fig. 1]

With decreased pulmonary blood flow, the arteries are smaller and the second order branches disappear in the mid-portion of the middle third of the lung. End-on vessels visualized near the hilum are few in number and smaller than their accompanying bronchi. [Fig. 2]

In increased pulmonary vascular resistance, the main and proximal pulmonary arteries are enlarged but the branches taper rapidly in the middle third of the lung giving the vasculature a pruned-tree appearance.

TABLE 1

CLASSIFICATION OF IMPORTANT MALFORMATIONS IN INFANCY

A. *Patients with Increased Pulmonary Flow*
    - Ventricular septal defect
    - Atrial septal defect
    - Persistent common atrio-ventricular canal
    - Patent ductus arteriosus
    - Aortico-pulmonary window
    - Anomalous pulmonary venous return
    - Transposition of the great arteries
    - Persistent truncus arteriosus

B. *Patients with Decreased Pulmonary Flow*
    - Tetralogy of Fallot
    - Severe pulmonary stenosis or atresia
    - Tricuspid atresia
    - Ebstein's malformation of the tricuspid valve

C. *Patients with Normal Pulmonary Flow*
    - Mild aortic stenosis
    - Mild pulmonary stenosis
    - Coarctation
    - Cardiomyopathies
    - Endocardial fibroelastosis
    - Aberrant origin of the left coronary artery

D. *Patients with Increased Pulmonary Resistance*
    - Pulmonary hypertension 1° or 2°
    - Transposition with VSD
    - Double outlet right ventricle

E. *Patients with Increased Pulmonary Venous Hypertension*
    - Anomalous pulmonary venous return with obstruction
    - Mitral atresia
    - Aortic atresia
    - Severe coarctation

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With venous hypertension the pulmonary capillaries and venules are enlarged and engorged with blood. If the capillary pressure exceeds the oncotic pressure of the blood, fluid may pass from the capillaries into the interstitial spaces and alveoli. The engorged vessels and surrounding transudate give the lung an increased radiodensity and the interstitial fluid may produce a reticular pattern. The edges of the vessels are ill-defined and blurred and on occasion septal lines may be seen. [Fig. 3]

a.) *Patients with Increased Pulmonary Blood Flow.*

In this group characterized by increased pulmonary vasculature, a number of cardiac anomalies must be considered (Table 1). The group can be further subdivided if one knows whether cyanosis is present or not (Table 2). The most commonly encountered anomalies are ventricular septal defect, atrial septal defect, patent ductus arteriosus, persistent common atrio-ventricular canal and partial anomalous pulmonary venous return. These five

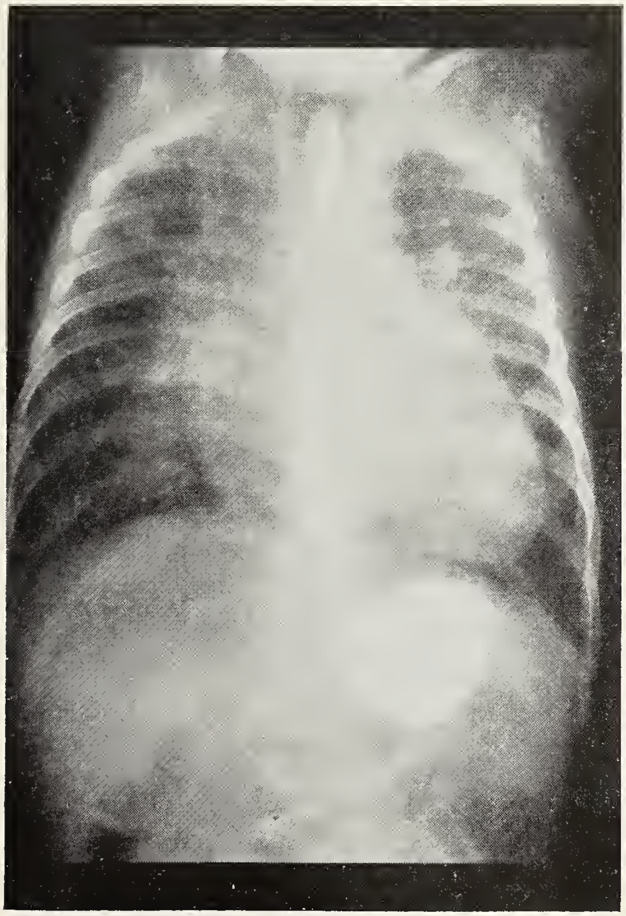

Figure 1

Increased vascularity in a patient with a ventricular septal defect and a large left to right shunt. Note vessels extending into the outer one-third of the lungs and the prominent main pulmonary artery.

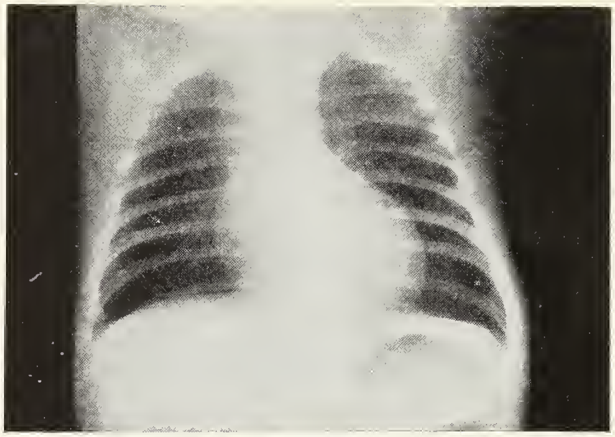

Figure 2

Decreased vascularity in a patient with pulmonary atresia. Flow to the lungs was via a small patent ductus. Note the small size of the vessels in the mid-portion of the lungs and the small hilar shadows.

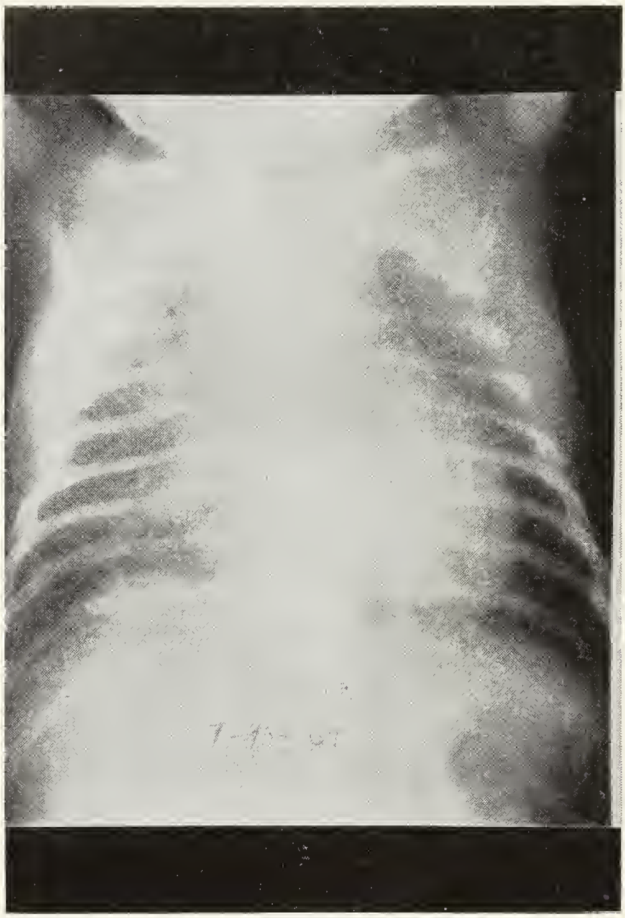

Figure 3

Venous obstructive pattern in a patient with total anomalous pulmonary venous connection to the azygos vein with obstruction. Note the diffuse haze over the lung fields, fluid in the minor fissure and the poor definition of vessels. There are septal lines at the right base.

TABLE 2

PATIENTS WITH INCREASED PULMONARY FLOW

A) Acyanotic
  1. Ventricular Septal Defect
  2. Atrial Septal Defect
  3. Patent Ductus Arteriosus
  4. Aortico-Pulmonary Window
  5. Persistent Common Atrio-Ventricular Canal
  6. Partial Anomalous Pulmonary Venous Return
B) Cyanotic
  1. Transposition of the Great Arteries
  2. Persistent Truncus Arteriosus
  3. Total Anomalous Pulmonary Venous Return

conditions comprise more than 50 percent of all cases of congenital heart disease. In infancy it is often difficult to separate these various entities radiographically. Estimation of ventricular size and left atrial enlargement, so often helpful in older children, is of little practical value in infants. Certain features may, however, be helpful.

1. If one does see left atrial enlargement one can exclude the diagnosis of atrial septal defect, since in this condition the left atrium can easily decompress itself into the right atrium and thus remains small even in the presence of a large left to right shunt.
2. If, in addition to increased flow, a prominent aortic knob is noted, a patent ductus arteriosus is most likely. Unfortunately, the aorta is often obscured by the thymus and cannot be seen in at least 50 percent of chest films in infancy.
3. If the degree of cardiomegaly is out of proportion to the increase in pulmonary vasculature, persistent common atrio-ventricular canal should be suspected. The bi-directional shunts and regurgitant valves in this condition may produce considerable cardiac enlargement.
4. A characteristic "figure of 8" appearance may be seen in anomalous pulmonary venous return to a left superior vena cava. The heart forms the lower half of the "8" while the large left and right superior venae cavae form the upper half (Fig. 4a, b).
5. If the pulmonary vasculature is increased, but the pulmonary artery segment is poorly seen, the diagnosis of transposition of the great arteries or truncus arteriosus should be considered. In transposition of the great vessels the heart often has a characteristic appearance, i.e. that of an "egg on its side." The pulmonary artery segment is often flat or concave and the base of the heart is frequently narrow due to the superimposition of the transposed aorta and pulmonary artery and the atrophy of the thymus that frequently ac-

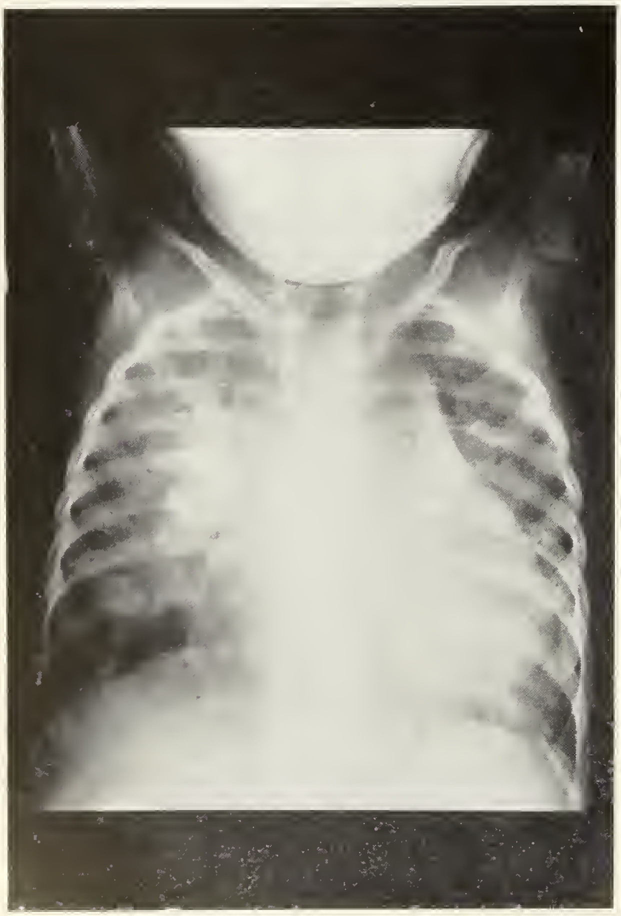

Figure 4a

Increased vascularity and widened superior mediastinum in a patient with total anomalous pulmonary venous return to a persistent left superior vena cava.

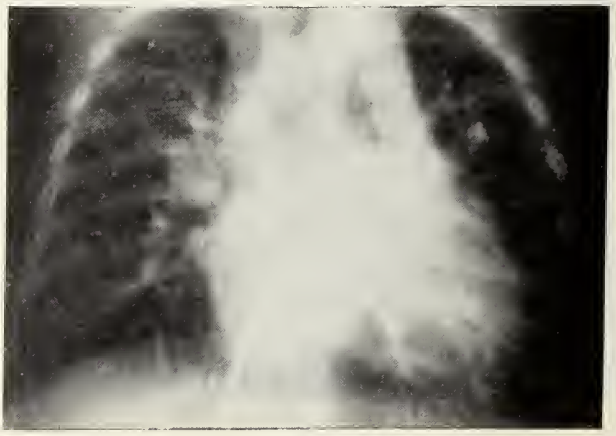

Figure 4b

Note the opacification of the left superior vena cava, the innominate vein and the right superior vena cava from the anomalously draining pulmonary veins.

companies this anomaly (Fig. 5). In persistent truncus arteriosus the pulmonary arteries arise from the ascending aorta either as a single structure or separately. Although the pulmonary arteries may be large, there is often no radiographic evidence of a main pulmonary artery.

6. A right aortic arch, in the presence of increased vascularity should suggest the diagnosis of persistent truncus arteriosus, since 30 to 50 percent of patients with truncus arteriosus have right-sided aortas.

b.) *Patients with Decreased Pulmonary Flow.*

Decreased pulmonary vasculature is usually seen in patients with obstruction to pulmonary arterial flow and a right to left shunt causing venous blood to bypass the lungs. The obstruction is usually at the level of the pulmonary valve, in the pulmonary outflow tract, or at the level of the tricuspid valve. The right to left shunt may be at the atrial or ventricular level. The commonest lesions in this group are tetralogy of Fallot, tricuspid atresia, severe pulmonary stenosis or atresia, and Ebstein's malformation of the tricuspid valve. These conditions may also be difficult to separate from each other but certain radiographic features are helpful.

1. The presence of decreased vascularity, an elevated apex and a right-sided aortic arch should suggest the diagnosis of tetralogy of Fallot since about 25 percent of cases have a right aortic arch. The classical "coeur-en-sabot" appearance although characteristic is seen in only about 30 percent of cases (Fig. 6).
2. If, in the presence of decreased vascularity, the left cardiac border is smooth and round, the right cardiac border is unusually straight and no interventricular notch is seen, the findings are suggestive of tricuspid atresia. The EKG is most helpful in differentiating patients with tetralogy from patients with tricuspid atresia since in tetralogy right ventricular hypertrophy is present while in tricuspid atresia left ventricular hypertrophy is seen.

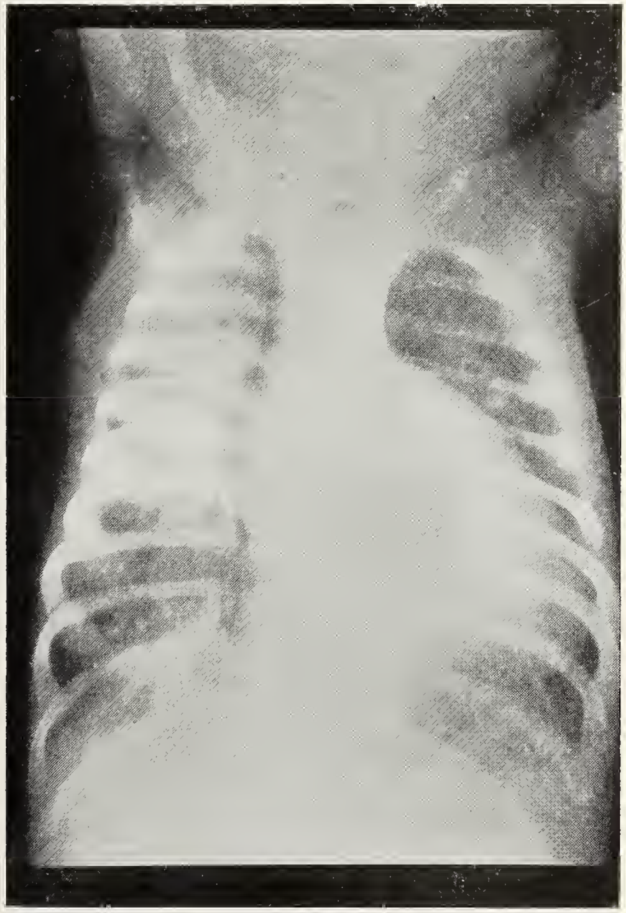

Figure 5

Patient with transposition of the great arteries. Note the "eggshaped" appearance of the heart, the narrow vascular pedicle and increased vascularity.

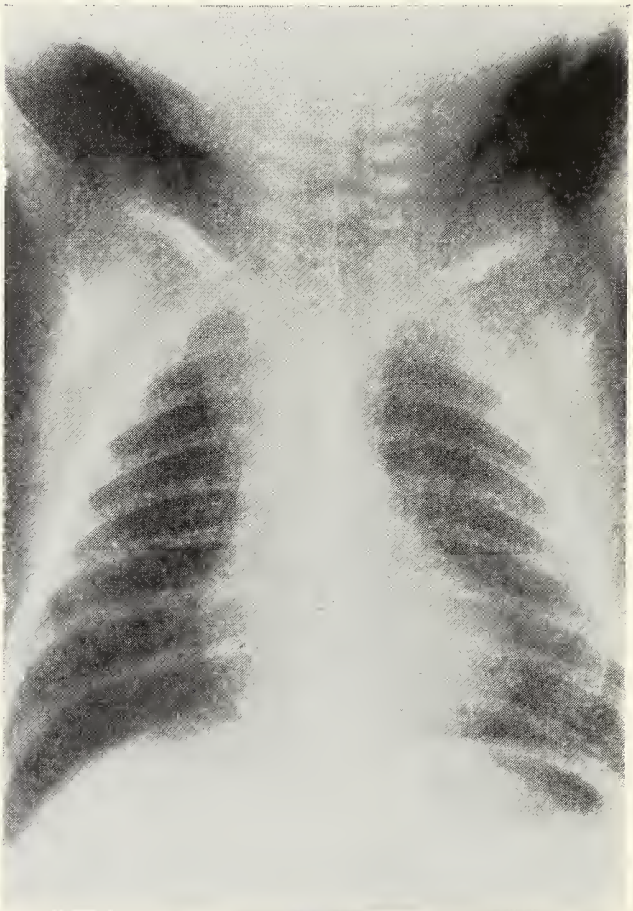

Figure 6

Decreased vascularity, elevated apex and right aortic arch in a patient with Tetralogy of Fallot.

3. With an enlarged heart and decreased vascularity one should consider the diagnosis of severe pulmonary stenosis or atresia. These patients usually have a fairly nonspecific X-ray, however.
4. A greatly enlarged globular heart with decreased pulmonary vascularity is characteristic of Ebstein's malformation of the tricuspid valve, an anomaly in which part of the tricuspid valve is displaced into the right ventricle making the valve incompetent. The globular appearance of the heart is produced by the massive right atrial enlargement and the upward displacement of the pulmonary outflow tract (Fig. 7).

c.) *Patients with Normal Pulmonary Vasculature.*

The commonest conditions in this group are mild aortic stenosis, mild pulmonary stenosis, coarctation, the cardiomyopathies, endocardial fibroelastosis, and origin of the left coronary artery from the pulmonary artery. It should be noted that any of the conditions in the other groups may have normal vascularity if mild in degree.

1. A normal appearing X-ray is usually seen in aortic stenosis, coarctation and pulmonary stenosis in this age group. The post-stenotic dilatation of the aorta or pulmonary artery seen in older children may not be seen in infancy since these structures are usually obscured by the thymus. The deformed aortic knob of coarctation is likewise often obscured and rib notching is rare before the age of 8.
2. An enlarged heart and normal vascularity may be indicative of endocardial fibroelastosis, origin of the left coronary artery from the pulmonary artery or a cardiomyopathy. The cardiac enlargement usually involves the left-sided chambers. (Fig. 8) It is usually impossible to differentiate between these conditions radiographically; but certain clinical features are helpful. Patients with anomalous origin of the left coronary artery usually have EKG evidence of an antero-lateral myocardial infarct. Patients with cardiomyopathies may have systemic evidence of the underlying process, e.g. the enlarged tongue and liver of glycogen storage disease.

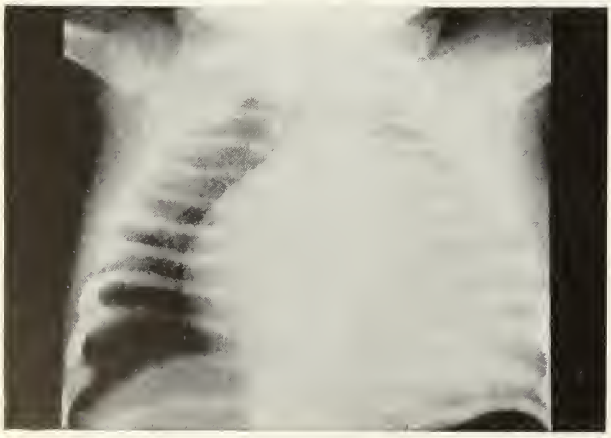

Figure 7

Typical appearance of decreased vascularity, and a markedly enlarged globular heart in a patient with Ebstein's malformation of the tricuspid valve.

d.) *Patients with Increased Pulmonary Vascular Resistance.*

This pattern is usually the end result of prolonged high flow to the lungs. It is usually secondary to large left to right shunts, transposition of the great arteries with ventricular septal defect or double outlet right ventricle. The pattern is not often seen in infancy since it takes some time for the roentgenographic features to develop. There are no characteristic features of the lesions in this group.

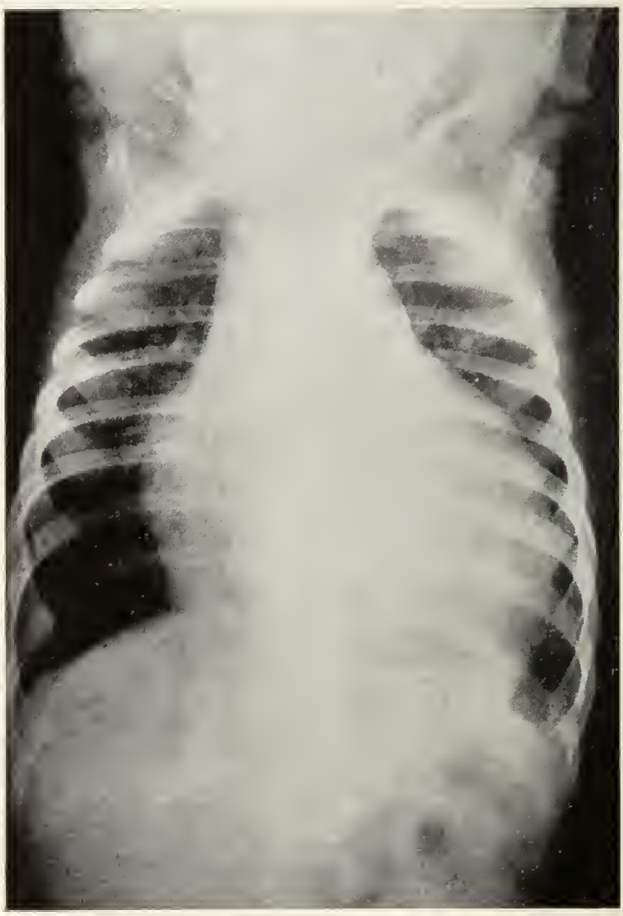

Figure 8

Endocardial fibroelastosis. Note the enlargement of the heart, especially the left ventricle. The vascularity is normal.

e.) *Patients with Pulmonary Venous Hypertension.* The commonest lesions in this group are anomalous pulmonary venous return with obstruction, aortic atresia, mitral atresia, and severe coarctation. Most of these patients present in the neonatal period and again it may be difficult to differentiate between them. Certain features will be helpful.

1. The combination of venous engorgement, septal lines and a small heart is characteristic of anomalous pulmonary venous return with obstruction (Fig. 3). In most cases, the anomalous vessels join a narrow common trunk which passes through the diaphragm to open into the portal system. Obstruction, however, can also occur with drainage into other structures such as the superior vena cava or azygos vein.
2. The pattern of venous engorgement and a large heart is seen most commonly in aortic or mitral atresia and severe coarctation (Fig. 9). It is often difficult to differentiate between these entities radiographically, but a difference in the pulses in the arms and legs should suggest the diagnosis of coarctation.

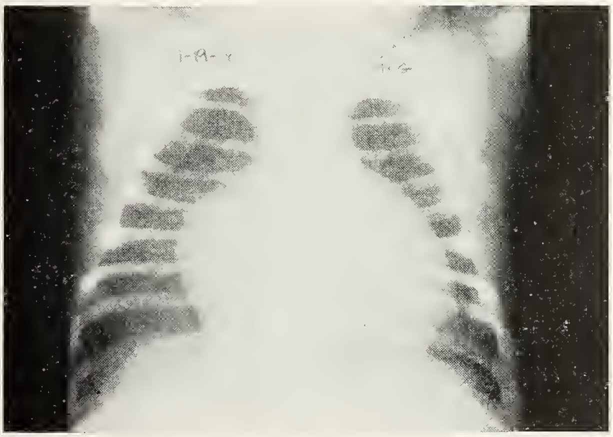

Figure 9

Enlarged heart and engorged ill-defined vessels in a patient with mitral and aortic atresia. Severe coarctation produces a similar picture.

Summary

The contribution of the chest X-ray in the diagnosis of congenital heart disease in infancy is variable. A radiological classification based on the appearance of the pulmonary vasculature allow subdivision into five broad diagnostic groups. Within each group correlation of the radiographic and clinical features frequently allows the correct diagnosis to be made.

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True Science teaches us to doubt and in ignorance to refrain.—*Claude Bernard.*

Anesthesiology and the Newborn For Cardiac Surgery

James I. Gilman, M.D.

The newborn with cardiac disease presents a complex problem of diagnosis and management. Even while the diagnosis is being made the infant may require intensive care. I will enumerate some of the major problems and explain how an anesthesiologist helps handle them. From the start I emphasize the importance of the involved physicians, cardiologist, pediatrician, surgeon, and anesthesiologist, combining their efforts in a team approach. The group aims to bring the child to anesthesia and surgery in the best possible condition.

The role of the anesthesiologist begins before arrival in the operating room. This association starts in the nursery or cardiac catheterization laboratory. As in the operating room, the anesthesiologist often is in the best position to view the entire situation. By his training, he is uniquely qualified to assess not only the state of ventilation, but also circulation and temperature regulation. When necessary he applies familiar techniques for assisting the infant in maintaining homeostasis.

Preoperative Care

Preoperatively we focus on three areas: body temperature, ventilation, and acid-base balance. The baby's disproportionally large surface area for his weight, and lack of peripheral vascular control, permit rapid heat loss. Keeping the child in an incubator most of the time, keeping him wrapped well, and keeping him on a heating blanket when he is out of the incubator will reduce or eliminate the excess heat loss. A portable thermistor allows constant monitoring. If the body temperature falls, circulation is compromised, and it becomes more difficult to rewarm the child.

Relatively few years ago, ventilation could be evaluated only roughly, by clinical judgement. Now we can quantitate ventilation by measuring blood gases. The test requires arterial puncture or an indwelling arterial line, but the technique produces results of such value as to justify the risk. Occasionally, we obtain satisfactory information with venous blood, but only for evaluation of levels of CO_2 and pH. Arterial blood alone will suffice for pO_2 measurements. There are not yet simple reliable methods for measuring tidal volume or minute volume on very small children.

The arterial pCO_2, or CO_2 tension, reflects the alveolar ventilation; normal arterial pCO_2 is 35 to 45 Torr, normal mixed venous pCO_2 is 5 to 7 Torr higher than arterial. A pCO_2 of 55 Torr indicates inadequate alveolar ventilation, and suggests that assistance is necessary. A pCO_2 above 60 Torr, or that is rising rapidly, indicates respiratory failure and requires vigorous assistance with a bag and mask. Often, a brief period of assistance will allow the infant to regain strength and maintain spontaneous ventilation again. However, if he can not sustain adequate ventilation, or there are other difficulties such as acidosis, hypothermia, or hypoxia, then the child needs intubation and assisted or controlled ventilation until diagnostic procedures are completed and definitive therapy begun. In some cases, artificial ventilation is maintained until the infant reaches surgery. A pressure limited ventilator, with infant attachment, such as the Bird,[R] will provide adequate ventilation. Maintaining an oxygen concentration of 40% is usually sufficient, although very hypoxic infants may need 100% oxygen prior to surgery.

Measurement of arterial pO_2 reveals the degree of hypoxia. Cyanosis is notoriously unreliable as an indicator of arterial oxygenation. The lighting in the room, as well as the state of peripheral perfusion and body temperature alter appearances so much as to make this clinical sign unreliable. Cardiac catheterization can provide right to left shunt values. Artificial ventilation, or at least respiratory assistance and periodic hyperinflation, reduce correctable atelectasis and maldistribution of gases, and reduce intra-pulmonary shunting.

Fetal hemoglobin has an oxygen dissociation curve to the left of adult hemoglobin, therefore, a low pO_2 may still provide adequate oxygen saturation. However, when the pO_2 falls below 25 Torr, even with high hemoglobin values, aerobic metabolism is not maintained, and metabolic acidosis oc-

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curs. Until improvement in ventilation or corrective surgery provides better oxygenation, only supplemental inspired oxygen will increase the arterial pO_2. When the shunt is large, even 100% O_2 will raise arterial pO_2 only a few Torr. Hyperventilation will lower the pCO_2, but can not overcome the hypoxia of shunts. In fact, hyperventilation in excess may worsen the situation by increasing the mean airway pressure and decreasing pulmonary flow.

Blood gas determination includes pH. The normal arterial pH is between 7.35 and 7.45. The child with hypoxia or poor peripheral perfusion may develop a metabolic acidosis as shown by a fall in pH and bicarbonate level. This decreases the perfusion even more, and may also contribute to hypothermia which compounds the problem. In addition, any form of respiratory depression or airway obstruction may elevate the pCO_2 and thereby lower the pH. Unless the cycle can be broken, arrhythmias or cardiovascular collapse occurs.

Therapy for acidosis includes reversing the causes for depression, anoxia, obstruction or hypothermia, and administration of a buffer solution. The simplest solution to use is standard 7.5% $NaHCO_3$ which contains 44.8 milliequivalents of bicarbonate in 50 milliliters. The serum bicarbonate level is measured directly, or calculated from the pH and pCO_2, and the deficit per liter of extra cellular fluid is calculated. The extra cellular fluid volume may be estimated as 30% of the body weight, and the appropriate number of milliequivalents administered. This will help improve cardiac contraction and peripheral circulation. The risk of cardiac arrhythmias or arrest from anesthesia is reduced when the pH is maintained near normal.

Premedication

When the cardiologist and surgeon decide that surgical intervention is required, the anesthesiologist determines premedication and anesthetic technique, based on the diagnosis and proposed surgery.

We keep premedication simple. Atropine 0.1 mg I M. provides vagal block, and prevents excess secretions. The peak time of action is about 20 minutes after I M administration, so that if a longer period intervenes, we repeat the dose. For infants of less than two kilograms weight 0.05 mg is adequate. If bradycardia occurs we repeat the atropine intravenously, in doses of 0.05 to 0.1 mg.

The child under six months does not need sedation. But if there are cyanotic spells, morphine sulfate provides good relief, in doses up to 0.1 mg/kg or occasionally as high as 0.2 mg/kg. If required, levallorphan tartrate reverses the respiratory depression caused by excess morphine in a ratio of 0.1 mg levallorphan tartrate for 1 mg morphine.

Anesthesia

During the anesthesia, the patient's condition is monitored constantly. Minimal monitoring consists of ECG by oscilloscope, blood pressure by cuff or arterial line and transducer, pulse or cardiac sounds by esophageal stethoscope, and temperature. Occasionally venous pressure is monitored, but the measurement is often unreliable. I find that palpating the anterior fontanelle gives as much information as obtaining a venous pressure by manometer and is much simpler.

Cardiac surgery requires general endotracheal anesthesia. I prefer to use a Bloomquist[R] infant circle-absorber system, with low flow of gases. This provides for easy control of respiration with CO_2 absorption and minimal heat loss. The closed or semi-closed system maintains a high humidity, near body temperature, to prevent drying of secretions.

Anesthetic agent selection depends in part on the condition of the patient, and in part on the equipment required for the surgery. When there is an explosion hazard, such as when cautery or cardiopulmonary bypass is required, then I employ a non-flammable, non-explosive agent. Nitrous oxide, oxygen, morphine and curare in varying combinations provide adequate analgesia and immobility for the surgery. When the degree of right to left shunt is great, a higher oxygen concentration with lower nitrous oxide concentration supplies the extra oxygen needed, and 0.1 mg increaments of morphine supplements analgesia. Curare will immobilize the patient, and reduce or stop diaphramatic movement, starting at a dose of 0.1 mg/kg.

Halothane and methoxyflurane are very potent anesthetics which are not explosive. They are particularly useful in the infant where hypoxia is not marked. However, these agents depress the myocardium directly, so I avoid them in patients with severe cyanosis or acidosis. On occasion, analgesic amounts of either halothane or methoxyflurane may be combined with oxygen and curare, producing adequate anesthesia with minimal cardiac depression.

When the cautery is not absolutely required, and there are no other explosion hazards, I prefer to use cyclopropane. It is potent, providing good analgesia, relaxation and respiratory control with a concentration between 10% and 30%. This allows for 70 to 90% oxygen concentration. Occasionally a small dose of curare is required, particularly if the degree of hypoxia is great, to reduce diaphragmatic movement. Because cyclopropane is relatively insoluble in the body, induction is more rapid than with the more soluble agents, and also, emergence is more rapid. When we expect the infant to be immediately benefitted by the surgery, and his general condition is good, rapid emergence is very desirable, it often allows early extubation.

Postoperative Care

Regardless of the agent and technique, we endeavor to extubate the infant as soon after surgery as possible. The problems of maintaining an infant on a ventilator are myriad, ranging from immobilizing the endotracheal tube properly, frequent trachael suctioning and frequent adjusting of the respirator, to avoiding tracheal trauma, providing proper humidity, and controlling oxygen concentrations.

If the curare required for surgery persists postoperatively, I prefer the child be left intubated, and allow him to metabolize and excrete the relaxant. Reversal of curare is possible with neostigmine after protecting against bradycardia and secretions with atropine. However, in general, I think it is less risky to maintain ventilation with artificial means until the drug is dissipated. Morphine in 0.1 mg increments will give enough sedation and central depression to keep the infant from fighting the respirator before the curare is totally removed.

If it is imperative to reverse the curare, then one may give atropine 0.015 mg/kg, followed by neostigmine 0.08 mg/kg, monitoring the cardiac rate and rhythm with constant ECG. Reversal will occur within 10 minutes. If it doesn't, other causes for apnea, or hypoventilation, must be sought, such as hypothermia, hypocarbia, hypotension, or electrolyte imbalance, particularly hyponatremia.

The various methods of measuring reversal of curare are not reliable in infants; it is not possible to get an accurate tidal volume or inspiratory force. Stimulation of peripheral nerves for twitch and tetanic response is also unreliable. General vigor and muscle tone, and ability to maintain adequate blood gases, are the best indicators of sufficient muscle strength for continued respiration and ability to cough and overcome a minor degree of airway obstruction. Constant close visual monitoring will provide the best safe guard against prolonged apnea or obstruction.

When we predict that the need for intubation will last longer than 24 hours, I replace the oral endotracheal tube with a nasal tube. The nasal tube lends itself to more convenient and reliable fixation, reducing the risk of accidental extubation or tracheal trauma from constant movement of the tube in the airway. If intubation is required beyond 72 hours, then tracheotmy is recommended.

Tracheotomy

Tracheotomy in the newborn may be a formidable undertaking, and should be avoided if simpler methods will suffice. However, with an endotracheal tube in place, and with adequate sedation and local anesthesia, or general anesthesia, a controlled situation may be achieved, allowing an unhurried procedure. The major problems arise after the tracheotomy. The newborn has a small airway, and there are no really satisfactory tracheotomy tubes for infants. The tube too small allows air leaks and renders positive pressure ventilation difficult, if not impossible. The tube too large will traumatize the trachea unduly. The newer polyvinyl chloride plastic tracheotomy tubes have reduced many of the problems of size and trauma, but they do soften at body temperature, and may slip out more easily. The classical metal tracheotomy tubes need a double cannula for cleaning, and therefore, have a very small inner or effective lumen for ventilation.

If all the problems of tracheotomy are successfully handled, when the child has recovered from his other surgery, it may still prove very difficult to remove the trachetotomy tube and get the infant to breathe adequately through his natural airways. Therefore, it may be necessary to care for the child with a tracheotomy for several months or years before decannulation is possible. Occasionally the complications of intubation and tracheotomy lead to permanent tracheal stenosis which requires trachael resection or a permanent tracheotomy.

Postoperatively, the anesthesiologist's role continues in the joint management of ventilation and airway control with the surgeons and cardiologists. Maintainance of a patient with a ventilator is very similar to the providing of artificial ventilation in the operating room, and the special skills of the anesthesiologist apply also in the recovery room and intensive care unit.

The management of ventilation and tracheobronchial care has progressed and improved over the past few years. It is possible to provide artificial ventilation for prolonged periods with relative ease. The ventilators are reliable and controllable, if some what expensive.

Regulation of inspired oxygen concentrations can reduce the risk of oxygen toxicity; returning to a concentration below 40% as soon as possible will lower the risk of pulmonary damage. An arterial pO_2 of 80 Torr is adequate, and if surgery has not eliminated the right to left shunt, a pO_2 of 40 to 50 Torr is acceptable. Transfusion to keep the hemoglobin levels above 15 to 18 grams/100 ml supplies adequate oxygen carrying capacity, even in the presence of desaturation.

Tracheal toilet, preceded and followed by hyperexpansion, removes excess secretions and eliminates bronchial plugging and atelectasis. Sterile technique, with gloves, and a new, disposable, catheter for every suctioning reduces the risk of contamination of the trachea. Gram negative organisms, many very resistant to antibiotics, are prevalent in intensive care units, so that sterile precautions are mandatory.

Humidification of all gases breathed by the infant will soften and liquify secretions, preventing crusting and plugging of tubes and airways. Heating the gases will reduce excess body heat loss, but care must also be taken to avoid causing over heating. Adequate humidification essentially eliminates respiratory fluid loss; calculation of daily fluid requirements must recognize the removal of this source of fluid loss.

The infant may experience the same difficulty in maintaining body heat stability postoperatively as preoperatively. Assistance includes using a warming blanket, eliminating drafts, keeping the infant covered, and warming intravenous fluids.

Summary

All measures taken in the care of the infant with cardiac disease are aimed at assisting homtostasis and eliminating extraneous stresses, allowing the body to expend energy more efficiently toward healing. An organized approach in this regard offers the best hope of success in his treatment. I have discussed several of the considerations of the anesthesiologist involved in treating such an infant.

There are two things of which all the well being of a state consists: the choice of a right end or inward action and the discovery of the means to achieve the end. Both the means and the end should be equally within our control. He said, "Take for example the art of medicine. Physicians do not always understand the nature of health and also the means which they use may not effect the desired end.—Aristotle

Cardiac Surgery in Infancy

H. C. Stansel, Jr., M.D.

Congenital cardiac lesions requiring surgical management during the first year of life are now well recognized conditions. The majority of the procedures are palliative operations designed to allow the child to survive until he is large enough to safely undergo more definitive corrections. These procedures are usually performed under more or less emergency conditions upon infants in relatively poor condition and require intensive pre and postoperative management to achieve acceptable survival rates. It is the purpose of this paper to describe the various procedures we have found useful in a variety of congenital cardiac defects.

It is useful to group the various defects into physiological categories because the surgical management is usually directed to the hemodynamic results rather than the specific cardiac anomaly. These are simply stated (1) excess pulmonary flow (2) decreased pulmonary flow (3) obstruction of either side of the heart or (4) inadequate mixing of the two circulations in transposition of the great vessels.

1) Excess pulmonary flow—

Conditions associated with large pulmonary flow may lead to heart failure or to irreversible pulmonary vascular disease. Patent ductus arteriosus occasionally presents in infancy producing sufficient pulmonary runoff to lead to heart failure and here division of the ductus produces a permanent cure. The majority of lesions, however, are more complicated when seen in the infant. Ventricular septal defect, endocardial cushion defects, single ventricle and a variety of other more bizzare lesions often defy definitive correction in the infant. Here, a palliative procedure, pulmonary artery banding, decreases pulmonary flow and allows compensation of the failing heart. This procedure, usually performed through a left thoracotomy, involves tying a heavy black suture around the pulmonary artery while monitoring aortic and distal pulmonary artery pressures. The objective is to lower the pulmonary artery pressure to near normal values without producing excessive arterial hypoxia by shunting too much venous blood out the aorta. When successful the infant rapidly achieves cardiac compensation with a decrease in the pulmonary plethora.

The child now has surgically created pulmonary stenosis which will become more severe with growth of the viscera. However, usually when the pulmonary stenosis becomes symptomatic the child is large enough to safely undergo other procedures designed to correct or further palliate the cardiac defect.

2) Decreased pulmonary flow—

There are a number of lesions associated with inadequate pulmonary blood flow. Tetralogy of Fallot, pulmonary stenosis or atresia, tricuspid atresia and other more complicated lesions often present with severe hypoxia associated with closure of the patent ductus arteriosus or increasing pulmonary outflow tract obstruction. These are highly fatal lesions when symptomatic in infancy and usually require the creation of extra cardiac shunts directed towards increasing pulmonary blood flow. During the first year of life the classic Blalock-Taussig anastomosis is seldom used because the small subclavian artery of the infant cannot deliver enough blood and the thrombosis rate is very high.

The most useful shunt procedure currently used is the Waterston-Cooley aortic pulmonary artery anastomsis. This procedure is readily performed even in the newborn and involves the creation of a side to side anastomosis between the right pulmonary artery and the ascending aorta. The size of the opening created is critical because too large a shunt is likely to lead to high output failure and too small a shunt will probably thrombose. It has been found that an anastomosis of about 5 mm. diameter is ideal but one must be aware that growth of the opening is likely with growth of the child. This may lead to excess pulmonary blood flow and eventually pulmonary vascular disease. It is, therefore, important to follow these children closely so that total correction or other palliative procedures may be performed before irreversible pulmonary vascular changes have developed.

The Potts-Smith anastomosis whereby the left pulmonary artery is anastomosed to the side of the descending aorta is also a useful procedure in selected cases. Because any systemic shunt must be closed at the time of total correction of the intracardiac defect, this shunt presents special problems. It is clearly the most difficult systemic-pulmonary shunt to close and, therefore, should be used

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in those lesions where total correction is most unlikely.

The superior caval-right pulmonary artery anastomosis or Glenn operation is useful in certain lesions in older infants. The small pulmonary arteries and high pulmonary vascular resistance of the infant preclude this anastomsis in the neonatal period. However, after three or four months of age this shunt offers excellent palliation in some cardiac defects. The most common lesions in which the caval-pulmonary artery shunt is used is tricuspid atresia and transposition of the great vessels associated with pulmonary stenosis. This shunt has the advantage of increasing pulmonary blood flow without increasing cardiac work and the low pressure characteristics are extremely unlikely to lead to pulmonary vascular disease. Although theoretically it is possible to totally correct some of the defects after establishment of the Glenn anastomosis, it would be a formidable procedure. It, therefore, should be considered as a permanent palliative procedure and should be used only in those lesions where total correction appears impossible.

3) Obstruction of either ventricle—

There are a variety of lesions producing obstruction of flow from the right or left ventricle. These include isolated aortic or pulmonary valve stenosis, hypoplastic right or left ventricle and coarctation of the aorta. These lesions may present as isolated defects but frequently are associated with other cardiac anomalies. Some of these defects are not correctable in infancy and require palliative procedures such as pulmonary valve stenosis associated with a hypoplastic right ventricle. Relieving the valve stenosis in this condition usually does not increase pulmonary blood flow due to the diminished stroke volume of the tiny muscle bound ventricle. A palliative procedure such as the Potts-Smith or Waterston-Cooley anastomosis will permit these infants to survive and some of them may actually become candidates for total correction. In the infant with isolated pulmonary valve stenosis and a normal or dilated right ventricular cavity, simple pulmonary valvulotomy performed under direct vision provided by inflow occlusion permits a permanent cure.

Isolated aortic valve stenosis producing symptoms in infancy is a highly fatal lesion. The markedly deformed valve usually found in this condition probably will become calcified if the child survives into adulthood but when symptomatic in infancy relief of the obstruction must be achieved. This is best performed under inflow occlusion where the thickened and deformed valve is merely incised to relieve the obstruction. A frequent complication of this form of repair is the production of some degree of aortic insufficiency. However, a moderate amount of leak is fairly well tolerated if the major lesion of obstruction is relieved. These children almost certainly will need further aortic valve surgery but at an age where open heart surgery is well tolerated.

Coarctation of the aorta leading to heart failure in infancy is a surgical disease. Resection and primary repair can be achieved even in the newborn with a low mortality. This lesion is frequently associated with ventricular septal defect. This combination of lesions presents special problems in that simple repair of the coarctation alone may not salvage the child. These infants present with left ventricular failure and high pulmonary venous pressure producing marked increases in pulmonary vascular resistance thereby limiting the left to right shunting through the ventricular septal defect. Left ventricular compensation following repair of the coarctation may sufficiently lower pulmonary vascular resistance to lead to marked increases in left to right shunting and subsequent high output failure. Therefore, when this combination of lesions coexist, repair of the coarctation and simultaneous banding of the pulmonary artery is indicated.

The infant with a hypoplastic left or right ventricle can be palliated significantly by techniques that tend to produce single ventricle physiology. The most common lesion producing the picture is tricuspid stenosis or atresia where most or all of the systemic venous return must pass through an atrial septal defect to the left ventricle. The pulmonary flow here may be markedly increased or severely limited depending upon the presence of a ventricular septal defect. Palliation here depends upon insuring the presence of an adequate atrial septal defect and providing optimal pulmonary flow. The atrial defect may be produced by the Rashkind balloon technique or by modifications of the Blalock-Hanlon procedure. Banding of the pulmonary artery or the creation of a systemic-pulmonary artery shunt depending upon the presence of over or under perfusion of the lungs will provide excellent palliation for these infants. Mitral atresia with ventricular septal defect or double outlet right ventricle are very similar lesions handled by the same techniques.

4) Inadequate mixing of the two circulations—

Transposition of the great vessels is a common lesion producing symptoms in the newborn. Survival here depends upon some defect where mixing of the pulmonary and systemic circulation may occur. Theoretically mixing can occur through an atrial septal defect, ventricular septal defect, or through a patent ductus arteriosus. Effective mixing, however, occurs only across an atrial septal defect and here creation of such a defect is life-saving. It is our practice to first attempt this by use of the Rashkind balloon technique. This procedure, when effective, produces excellent palliation at low risk and also has the advantage of leaving the pericardial space free of adhesions. This is especially important when the child is old enough for definitive repair where the pericardium is used to create an atrial baffle by the technique of Mustard. However, we and others have noticed a high incidence of failure of the balloon technique and these infants are treated surgically.

We currently prefer to create the atrial defect by direct vision intracardiac surgery under conditions of inflow occlusion at normal body temperatures. If the child also has an associated ventricular septal defect, then simultaneous pulmonary artery banding is performed. When pulmonary stenosis coexists with transposition it may be necessary to create a Waterston-Cooley type of systemic-pulmonary artery shunt at the time of atrial septostomy.

It is clear from the above discussion that any intelligent surgical management depends upon accurate demonstration of the anatomy of the cardiac defect. Close cooperation between the pediatric cardiologist, the radiologist, and the surgeon is necessary to provide this information.

Intensive pre and postoperative management is vital if these critically ill infants are to survive. Because of the lethal nature of many of these lesions, correction of metabolic acidosis is frequently all that can be achieved before operative intervention. This is most often the case where inadequate pulmonary flow and severe hypoxia are the presenting findings. The infant with pulmonary flooding or obstruction due to coarctation or other similar lesions may be markedly improved by digitalization in preparation for surgery.

Immediately prior to surgery an indwelling arterial line is placed in the abdominal aorta via the profunda femoris artery. This permits continuous monitoring of arterial pressure as well as frequent determinations of arterial blood gases and acid-base studies. Cardiac action is carefully followed by continuous electrocardiographic tracing and meticulous attention is paid to exact blood replacement.

During the postoperative period respiratory insufficiency is frequently encountered in the infant. It is only with the use of assisted or controlled respiration carefully evaluated by changes in arterial blood gases that permit many of these patients to survive.

Despite the tremendous problems presented by these severely ill infants, acceptable results can be achieved by intensive pre and postoperative care and exacting operative techniques. We can currently expect at least 70 per cent of all infants with lethal cardiac disease to survive palliative or curative cardiac surgery during the first month of life.[1]

Summary

This paper has attempted to briefly describe the methods currently available to provide palliation or cure of serious cardiac disease in the infant. At the present time almost every infant with a cardiac defect can theoretically have some surgical procedure which will permit survival for a time. It is true that many of these youngsters need further surgical procedures as growth occurs. The time should certainly be past, however, when a family is told that nothing can be done to help their child with serious cardiac disease. Also, developments which almost certainly will come are destined to open further possibilities in the management of the infant with a serious congenital heart defect.

[1] INFANT CARDIAC SURGERY—1969-1970

Diagnosis	*Operation*	*Age*	*Result*
1. Patent Ductus Arteriosus	Ligation & Division	21 da.	A
2. Total Anomalous Pulmonary Venous Drainage with Venous Obstruction	RPV-SVC Anastomosis; Atrial Septostomy	8 da.	D
3. Ventricular Septal Defect	Pulmonary Artery Banding	3 mo.	A
4. Transposition of Great Vessels, Pulmonary Stenosis	Atrial Septostomy; RPA-AO Anastomosis	1 da.	D
5. Tetralogy	Pulmonary Artery to Aortic Anastomosis	3 mo.	D
6. Congestive Heart Failure, Atrial Septal Defect, Ventricular Septal Defect	Pulmonary Artery Banding	20 da.	D
7. Tetralogy	Cooley	6 mo.	A
8. Transposition of Great Vessels	Atrial Septostomy	5 da.	A
9. Hypoplastic Left Ventricle; Patient Ductus Arteriosus, Aortic Stenosis	Cooley Shunt, Blalock-Hanlon, Pulmonary Artery Banding	18 da.	A
10. Coarctation, Patient Ductus Arteriosus, Ventricular Septal Defect	Resect. Coarct., Ligation & Division, Pulmonary Artery Banding	1½ mo.	A
11. Endocardial Cushion Defect	Pulmonary Artery Banding	4 mo.	D
12. Tetralogy	Cooley	4 mo.	D
13. Patent Ductus Arteriosus	Ligation & Division	1 mo.	A
14. Coarctation	Resection	2 mo.	A
15. Patent Ductus Arteriosus	Ligation & Division	10 da.	D
16. Transposition Great Vessels	Atrial Septostomy	6 da.	A
17. Transposition Great Vessels	Atrial Septostomy	2 da.	A
18. Tetralogy, thrombosis Right Pulmonary Artery	Thrombectomy Left Pulmonary Artery, Potts-Smith Anastomosis	6 mo.	A
19. Pulmonary Atresia	Atrial Septostomy	3 da.	D
20. Ventricular Septal Defect	Pulmonary Artery Banding	2 mo.	A
21. Transposition Great Vessels, Single Ventricle Pulmonary Stenosis	Potts-Smith Anastomosis	5 da.	A
22. Endocardial Cushion Defect	Pulmonary Artery Banding	8 mo.	A
23. Transposition Great Vessels, Ventricular Septal Defect	Atrial Septostomy	4 mo.	A
24. Ventricular Septal Defect, Atrial Septal Defect	Pulmonary Artery Banding	1½ mo.	A
25. Double Outlet Right Ventricle with Ventricular Septal Defect, Atrial Septal Defect	Pulmonary Artery Banding	1 mo.	A
26. Transposition Great Vessels, Pulmonary Stenosis	Potts-Smith Anastomosis	2 da.	A
27. Coarctation, Patent Ductus Arteriosus	Repair, Ligation & Division	9 da.	A
28. Pulmonary Stenosis with Hypoplastic Right Ventricle	Potts-Smith Anastomosis	2 da.	A
29. Tricuspid Atresia	Potts-Smith Anastomosis	2 da.	A
30. Tricuspid & Pulmonary Atresia	Potts-Smith Anastomosis	1 da.	D
31. Hypoplastic Left Heart, Ventricular Septal Defect, Patent Ductus Arteriosus	Banding Left & Right Pulmonary Artery	1½ mo.	A
32. Tetralogy	Cooley	6 mo.	A
33. Coarctation, Patent Ductus Arteriosus, Ventricular Septal Defect	Repair, Ligation & Division	1 mo.	A
34. Transposition Great Vessels	Atrial Septostomy	3 da.	A
35. Aortic Atresia	Potts-Smith Anastomosis, Pulmonary Artery Banding	2 da.	D
36. Ventricular Septal Decet	Pulmonary Artery Banding	4 mo.	A
37. Transposition Great Vessels	Atrial Septostomy	1 da.	A
38. Hypoplastic Right Heart	Potts-Smith Anastomosis	3 da.	A

Results—38 Cases
10 Deaths
26% Mortality

THE PRESIDENT'S PAGE

One of the goals of the Connecticut State Medical Society is to help its members provide the people of Connecticut with the highest quality of medical care at reasonable cost. How the quality of medical care is measured varies with the individual. This is also true when different groups of health professionals discuss quality. In my previous President's Page, I discussed some of the methods of delivering medical care. The proponents of each of these methods claim their method provides the highest quality of medical care.

The first criterion of quality must be availability, for no matter how high the quality, it is of no value if it is not available. To be of high quality, medical care must be available in terms of distance as well as time. When it is available only between certain hours or on certain days, the level of quality, of necessity, is lower.

A second criterion of quality is professional competence. As practicing physicians we think of professional competence in terms of correctly diagnosing the patient's condition and instituting the proper treatment. To the patient the latter is most important, for his prime concern is to recover from his illness as quickly as possible. He may or may not be particularly concerned whether numerous sophisticated and expensive laboratory examinations are performed to establish the diagnosis, as long as he recovers.

This definition of professional competence may be a little simplistic but it is offered in order to stress the importance of the welfare of the patient when devising methods of measuring professional competence. Peer Review such as the medical and surgical audits presently performed in many hospitals can be helpful in evaluating competence. A modification of this mechanism could be used for the ambulatory patient. Peer Review is not perfect since the reviewers cannot be omniscient, especially where ambulatory patients are concerned. However, it appears to be the best method available at present.

A third criterion of quality is one that the patient has recently voiced and which previously was taken for granted, namely personal interest and concern. With the changes taking place in the methods of delivery and in the providers of medical care, there has been a trend toward impersonal care. While some of the advocates of these changes have recognized this, they have not found it undesirable. However, the patient today does want more than cold scientific competence from his physician. He desires a certain amount of personal concern and compassion and, wherever possible, an explanation of his condition and the procedures both diagnostic and therapeutic that will be performed.

A fourth criterion of quality is continuum of care or follow-up care. The best follow-up care is that which is rendered by the same physician. When the follow-up care is rendered by two or more physicians it is necessary that the medical records be available to all physicians concerned and that the record keeping be meticulous. If this is not the case the quality must be poorer.

The above are some of the criteria for measuring the quality of medical care from the viewpoint of the patient who receives the care and from the physician who provides the care. In evaluating various methods of delivering medical care their proponents have suggested other criteria. These have included the number and variety of laboratory (including radiologic) examinations and the quality of the record-keeping. While the former are important when medically indicated and relevant to the patient's problem, this has not always been considered.

Morris A. Granoff, M.D.

FROM THE EXECUTIVE DIRECTOR'S OFFICE

160 St. Ronan Street, New Haven, Conn. 06511
Telephone 865-0587

Raymond T. Sullivan, Jr.
Assistant Executive Director
Public Affairs

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Executive Director
Josephine P. Lindquist
Associate Executive Director

Leonard R. Tomat
Assistant Executive Director
Scientific Activities

SUMMARY OF ACTIONS COUNCIL MEETING

Thursday, June 4, 1970

I. Attendance

Present were: Drs. Granoff, Weber, Jr., Grendon, Burnham, Edson, Brandon, Abbot, Martin, Dean, Gardner, Fabro, Rem, Cramer, McDonald, Pelz, Palomba, Roch, VanSyckle, Johnson, Ragland, Jr., Freedman, Root, Jr., vonGlahn, Purnell and Klare.

Also present were: Mrs. Lindquist, Mr. Sullivan, Mr. Tomat, Mr. Donelan (AMA), Mr. Gordon (HCMA), Mr. Olson (FCMA), Dr. Hess (Welfare Medical Director), Dr. Polivy (Liaison Committee with Welfare Department), Dr. Wright (CAGP) and Dr. Richards.

Absent were: Drs. Harwood, Wilson, Jr., Nemoitin, Friedberg and Gorin.

II. Organization

Following opening remarks by the President, Dr. Granoff, and the introduction of members and guests, the elections of a Chairman and Vice-Chairman for 1970-71 were held. Without contest, Stevens J. Martin, Hartford, was elected Chairman and Kenneth F. Brandon, Hartford, Vice-Chairman.

III. Routine Business

Approval of Minutes

As printed and distributed, it was VOTED to approve the minutes of the meeting of April 29, 1970.

Life Memberships

It was VOTED to approve applications for Life Membership received from the following eligible Active Members:

Joseph Becker, 302 State Street, New London (NLCMA)—1971

Edward Gipstein, 181 Broad Street, New London (NLCMA)—1970

Appointments

(a) *Public Affairs Division:* In keeping with a subject amendment to the Bylaws (5/12/70), the Divisional Board for the new Public Affairs Division was appointed as follows:

Chairman—

Bernard A. Burnham, Waterbury
Chairman, Committee on National Legislation

Isadore H. Friedberg, Newington
Chairman, Committee on State Legislation

James H. Root, Jr., Waterbury
Chairman, Committee on Public Relations

Kenneth F. Brandon, Hartford
Chairman, Committee on Public Affairs

(b) *Committee on State Legislation:* In keeping with a subject amendment to the Bylaws (5/12/70), additional members were appointed to the Committee on State Legislation for 1970-71 as follows:

From FCMA:

Eugene H. Corley, Bridgeport, Bernard O. Nemoitin, Stamford, Louis Rogol, Danbury.

From LCMA:

Francis Gallo, Winsted.

From HCMA:

Max R. Goldstein, Hartford, Phillip E. Trowbridge, Hartford; Charles Polivy, Hartford.

From NHCMA:

Jerome K. Freedman, New Haven; James H. Root, Jr., Waterbury.

At-Large:

Phillip A. Shelton, Hartford—Section on Ophthalmology; Manny Myerson, Hartford—Section on Otorhinolaryngology.

(c) *Committee on Public Health:* It was VOTED to appoint Benjamin Levy, Hartford, to membership on this Committee.

(d) *Committee on Professional Liability:* It was VOTED to appoint J. Alfred Fabro, Torrington, as the Council representative on this new Committee, and to name Dr. Fabro chairman of the Committee. The other members are (by title): Chairman of the Judicial Committee (Dr. Fabro), Chairman of the Conference Committee with the State Bar Association (also Dr. Fabro), Chairman of the Committee on Public Relations (James H. Root, Jr., Waterbury), Chairman of the Committee on Medical Economics and Insurance (M. David Deren, Bridgeport), Chairman of the Committee on Hospitals (Christie E. McLeod, Middletown), Chairman of the Committee on State Legislation (Isadore H. Friedberg, Newington), and the chairmen (one each) of the County Medical Associations' Committees that handle malpractice situations (by whatever name).

Date of Next Meeting

The date for the next meeting of the Council was set for Wednesday, July 15, 1970.

IV. Old, New and Special Business

Requests for Expenditures

It was VOTED to allocate to the budget of the Committee on National Legislation up to $1,500 to cover the anticipated costs of a "Congressional contact" visit to Washington, D.C. in July, such visit to be made by a delegation of members of the Committee on National Legislation, CSMS officers and staff personnel and several at-large members (from other committees, etc.)

Communication—New Haven County Medical Association

The Board of Governors of the NHCMA reminded the Council of a matter referred to it more than a year ago, for study and recommendation, to which the Council has not made a definitive response. In brief, the matter concerned the complaint of an NHCMA member that, in handing down a judgment in an accident case, the judge made critical comments regarding the member's charges which were irrelevant to the decision and totally unwarranted in light of the reasonable nature of the charges made. The Council had referred the matter, for study and report, to the Conference Committee with the State Bar Association. It was VOTED to request the Conference Committee with the State Bar Association to arrive at a definitive conclusion with respect to the question raised by the NHCMA member and Board of Governors and to report on same to the Council at the earliest time possible.

Report—Committee on Public Health

It was VOTED to accept the report of the Committee concerning approval, for CSMS exhibiting and advertising, of the following out-of-state clinical laboratories: The Boston Medical Laboratory, Boston, Massachusetts; The Metropolitan Laboratory, Teaneck, New Jersey; and the Biochemical Procedures Laboratory, Los Angeles, Cal., the Committee having evaluated these laboratories in accordance with criteria established by the Council several years ago. As to the Committee's recommendation that the laboratories should be "required to bill each patient and not the referring physician for services", it was VOTED to refer this recommendation back to the Committee for further study; i.e., whether such a requirement can and/or should be imposed on *all* clinical laboratories, instate or out-of-state.

Report—Ad Hoc Committee to Study Hospital Costs

It was VOTED to accept, with commendation, a report of this Ad Hoc Committee concerning hospital costs and related matters, with the addition of a statement recommending that third party payors should be encouraged to increase prepaid coverage for outpatient medical workups in order to eliminate the necessity for expensive hospital admissions to qualify patients for benefits payments for such workups. It was further VOTED to refer the report to the Committee on Hospitals for intra-committee study and also for joint discussion with the Connecticut Hospital Association's Council on Professional Practice, with subsequent report to the Council. In addition to the report proper, a commentary submitted by Kurt Pelz, Wallingford, a member of the Ad Hoc Committee is to be transmitted to the Committee on Hospitals for information and discussion.

Progress Report—Coordinating Committee on U&C Charge programs

It was VOTED to accept as information a copy of the minutes of a May 6 meeting of the Coordinating Committee which, among other things, reported the Committee's intention to develop utilization criteria for various categories of disease entities which could be used as guidelines for judging the quality of care being delivered by a practitioner in terms of good medical practice. Since the Committee chairman, Sidney L. Cramer, stated that he felt that the treatment of cardiovascular conditions would be a suitable category to start on, it was VOTED to request the County Association Councilors to submit to Dr. Cramer (or the CSMS office) the names of three qualified cardiologists practicing in their county areas. From these names, Dr. Cramer will form a committee to develop the utilization criteria.

Progress Report—Committee on Third Party Payments

Presented by James H. Root, Jr., Chairman, the Committee on Third Party Payments filed with the Council a report on its progress toward "updating" the present official CSMS Relative Value Scale and made a series of recommendations designed to bring this long standing project to completion. After brief discussion, the Council VOTED to approve these recommendations as follows:

(1) That a revised RVS be made up of five separate sections (instead of the present four): Medicine, Surgery, Anesthesia, Radiology and Pathology.

(2) That the revised sections on Medicine and Surgery be based on the format of the new, 1969 California Relative Value Studies.

(3) That, if (1) and (2) are approved, the CSMS Sections and allied groups which have expressed interest in making changes in the RVS be asked to write the desired changes into their copies of the 1964 California Relative Value Studies (official CSMS Relative Value Scale) by mid-September, 1970.

(4) That the staff of CSMS (with additional staff assistance if needed), in consultation with the Committee on Third Party Payments, prepare the revised material for publication in a CSMS-published RVS manual.

(5) That the Council commit up to $7,200 of contingency and/or reserve funds for the future publication of 7,500 copies of a CSMS Relative Value Scale which will contain all revisions made in accordance with (1), (2) and (3) above.

Medicaid Program

(a) It was VOTED to receive as information copies of the "corrected" minutes of the March 12 meeting of CSMS representatives and others with Subcommittee III of the General Assembly's Health Care Study Committee. The original version, prepared by the Subcommittee's staff, had been quite misleading insofar as recording the points of view, comments and proposals advanced by the Society's representatives. Copies of the corrected minutes have been mailed to all who participated in the meeting of March 12, 1970.

(b) It was VOTED to table action on a proposal that the Council appoint (or make nominations for) a new Medical Advisory Committee to work with the Welfare Medical Director in the administration of a new payment program which is supposed to become effective on July 1, 1970. In accordance with a directive of the House of Delegates (May 12, 1970), the County Medical Associations have been requested to nominate at least five members each to be considered by the Council for transmission to the Commissioner of Welfare for his appointment.

(c) John C. Wright, Manchester, president of the Connecticut Academy of General Practice, joined the Council to report on a meeting of CAGP representatives with the State Professional Policy Committee and staff, on June 3, 1970, at which strong objections were voiced by the Academy's representatives with regard to several features of the PPC's proposed new payment mechanism for physicians' services rendered to Medicaid beneficiaries; objection to a "fixed fee" schedule, rather than a flexible payment method; objection to "duality of payments" between generalists and specialists; and objection to offering physicians practicing in the Tolland-Windham County area less than they are receiving currently and since March 1, 1969. Charles Polivy, Hartford, chairman of the Council's Liaison Committee with the Welfare Department, also joined the Council to discuss the proposed new program, as did Orvan W. Hess, Welfare Medical Director.

In the course of the lengthy discussion of this matter that ensued, it became clear that, based on the information which had been made available to the Society as of the time of this meeting, there were a number of features embodied in the proposed schedule which were subject to being misunderstood and that, in fact, many of these may have already been misinterpreted by members of the Council as well as (or so it appeared) by representatives of the CAGP. Both Dr. Polivy and Dr. Hess explained the intended application of these features in such a way as to place an entirely different light on the program from what the previously received communications from the

Professional Policy Committee seemed to have projected. While it is doubtful, despite the extended discussion of the subject, that a single "understanding" among all those participating was reached on all features of the proposed schedule, it appeared to the Executive Director that the following points were developed as reasonably factual:

(1) All covered physicians' services will be assigned code numbers and unit values in accordance with the 1965 CSMS Relative Value Scale. The CMS Preferred Contract will be eliminated as the basis for payments for surgical services.

(2) The principle of prevailing levels of charges, developed from data accumulated during the 1968-69 trial year of "usual and customary charges", will be used as the basis for determining the payments to be made for services rendered by physicians in all types of practice. There will be no "fixed" or "uniform" fee schedule, published or unpublished.

(3) Complying with a directive of HEW, the "prevailing levels" of allowable charges will be set *at the 75th percentile as of January 1, 1969*. Prior to that date, these levels were set at the 83rd percentile.

(4) Practitioners submitting claims for payment will be required to indicate as "usual charges" *those charges that were claimed for payment prior to January 1, 1969; not* usual charges made subsequent to that date or currently.

(5) The same reduction in the 1/1/69 prevailing levels of charges (from the 83rd to the 75th percentile) will apply equally to all practitioners in all types of practice. In no case will a physician receive payment higher than that based on the usual charge he claimed for payment prior to January 1, 1969. In some cases, the payment may be less because the "prevailing levels" of allowable charges will now be set at the lower 75th percentile.

In any event, the Council VOTED to direct the Liaison Committee chairman to seek to arrange a meeting of the Committee with the Professional Policy Committee as soon as practical, at which meeting the Liaison Committee is to inform the Commissioners of Welfare and of Finance and Control (who comprise the PPC) of recent actions by the Council and House of Delegates which have bearing on the question (opposition to a "fixed" schedule; opposition to "duality of payments" under a fixed schedule) and to reaffirm the Society's position that only a flexible payment method based on the "usual and customary charge" principle will be satisfactory to the Society.

N.B.: *The foregoing is a summary of the proceedings and actions of the Council on June 4, 1970. Detailed minutes of the meeting are on file at 160 St. Ronan Street, New Haven, for perusal by any interested member of the Society.*

Placement Wanted

INTERNIST—31 years of age, Eligible with National Boards, wishes solo, group or associate type practice in Connecticut. Interested in the area along the southern coast of Connecticut between 40 and 120 miles from New York City.

PHYSICAL MEDICINE AND REHABILITATION-ELECTRO NEUROMYOGRAPHY DIAGNOSIS—44 years of age, Board eligible, wishes group, associate or full time institution practice. Available mid-summer.

ANATOMIC PATHOLOGY—38 years of age, Certified, wishes to practice in Connecticut. Military obligation completed. Available immediately.

ANESTHESIOLOGY—56 years of age, Certified, wishes group, associate, institutional or industrial type practice in Connecticut. Available immediately.

PHYSICIAN-COLLEGE HEALTH — 26 years of age, with National Boards, wishes group or associate type practice in Connecticut.

OB & GYN—37 years of age, Certified, wishes associate or group type practice in Connecticut. Presently in practice with Connecticut license.

PHYSICIAN—26 years of age, wishes group type practice in Connecticut. Available mid-summer.

INTERNIST—32 years of age, Eligible with National Boards, wishes group or associate type practice in Connecticut. Seeking a position in internal medicine with an emphasis on chest disease preferably associated with a hospital where he can provide pulmonary function testing and good respiratory care.

ANATOMIC & CLINICAL PATHOLOGY — 34 years of age, Eligible with National Boards, wishes solo or associate type practice in Connecticut. Military obligation completed.

SURGEON—32 years of age, Eligible with National Boards, wishes solo, group or associate type practice in Connecticut.

INTERNAL MEDICINE-GASTROENTEROLOGY—31 years of age, Eligible with National Boards, wishes group or associate type practice in Connecticut.

PEDIATRICIAN—30 years of age, Board Eligible with Connecticut license. Desires associate type practice in Connecticut leading to partnership with another pediatrician or group practice.

INTERNIST—38 years of age, Certified with National Boards, wishes solo or associate type practice in Connecticut. Presently in practice. Military obligation completed. Available immediately.

ANESTHESIOLOGIST—36 years of age, Certified, wishes group, associate or institutional type practice in Connecticut. Seeking position where he could use his experience in respiratory care and anesthesia for cardio-pulmonary surgery. Presently in practice.

UROLOGIST—34 years of age, Certified, wishes group or associate type practice in Connecticut. Presently in practice.

OBSTETRICS AND GYNECOLOGY—35 years of age, Eligible with Connecticut license, wishes group, associate or institutional type practice in Connecticut.

OPHTHALMOLOGIST—49 years of age, Certified, wishes solo type practice in Connecticut. Presently in practice, Military obligation completed.

INTERNIST—31 years of age, Certified with National Boards, wishes solo or group type practice in Connecticut. Presently in practice. With Connecticut license.

PEDIATRICIAN—39 years of age, Certified with Connecticut license, wishes institutional type practice in Connecticut. Available now.

OPHTHALMALOGIST—39 years of age, Certified with National Boards, wishes solo or associate type practice in Connecticut. Presently in practice. Military obligation completed. Available anytime.

INTERNIST—34 years of age, Eligible, wishes to practice in Connecticut. Military obligation completed.

PATHOLOGIST—38 years of age, Certified, wishes group type practice in Connecticut.

SURGEON—33 years of age, Certified with National Boards, wishes group or associate type practice in Connecticut. Presently in practice. Available immediately.

GENERAL PRACTICE—59 years of age, Eligible with Connecticut license wishes group, associate, institutional or industrial type practice in Connecticut. Available immediately.

INTERNIST—36 years of age, Eligible with National Boards, presently in practice wishes solo type practice in Connecticut. Available in the fall.

THORACIC AND CARDIOVASCULAR SURGERY—36 years of age, presently in practice, wishes group or associate type practice in a large community in Connecticut. Primarily interested in thoracic and cardiovascular surgery but would be interested in combining this with general surgery. Available immediately.

ANESTHESIOLOGY — 45 years of age, Eligible with National Boards, wishes group, associate, institutional or industrial type practice in Connecticut. Available immediately.

ANESTHESIOLOGY—37 years of age, Eligible, presently in practice, wishes solo, associate or group type practice in Connecticut. With Connecticut license Available immediately.

INTERNIST—33 years of age, Eligible with National Boards, wishes group or associate type practice in Connecticut. Available in October.

OPHTHALMOLOGIST—31 years of age, Certified with National Boards, wishes solo, group or associate type practice in Connecticut. Available immediately.

INTERNIST—36 years of age, Certified with National Boards, wishes group or associate type practice in Connecticut. Available in August.

ANYONE INTERESTED IN THE ABOVE IS ASKED TO CONTACT THE PHYSICIANS PLACEMENT SERVICE, 160 ST. RONAN STREET, NEW HAVEN, CONNECTICUT 06511.

Placement Opportunities

GENERALIST wanted to take over lucrative practice in southeastern Connecticut village. Excellent opportunity for semi-retired physician. Box 95, Old Lyme, Connecticut 06371.

NEW MILFORD, CONN. community hospital of 79 beds, with an ICCU and planned expansion to 150 beds. Located on Candlewood Lake, one hour from Long Island Sound, and one and one half hours from New York City. We have a rapid population growth rate, excellent schools, and skilled-level industry. Further details are available from Dr. Randall Hays, M.D., Chief of Staff, New Milford Hospital, New Milford, Connecticut 06776.

PHYSICIANS needed in the following general specialties: Allergy, Anesthesiology, Dermatology, Internal and General Medicine, Psychiatry, Gastroenterology, and Otorhinolaryngology to practice in Torrington, Connecticut and surrounding communities. Modern 191 bed general, short term, voluntary, hospital, with all major medical and surgical specialties represented, serves a population of 50,000. Need to augment the Medical Staff due to immediate past and future retirement of active members of the Medical Staff as well as anticipated population increase during the next 10 years. Hospital is located in the center of Litchfield County, one of the most scenic parts of New England. Area offers excellent recreational facilities and is one hour from New Haven and Hartford, two hours from New York, and three hours from Boston. Search Committee of the Medical Staff will assist qualified candidates. Write or call: Thomas H. Walker, M.D., Chairman of Search Committee, The Charlotte Hungerford Hospital, Torrington, Connecticut 06790. Phone: (203) 489-0441.

MEDICAL OFFICE, its furniture and patient's records of internist leaving his practice for full time job, will be available at the end of June 1970 in Stratford, Connecticut.

PEDIATRICIAN—Partner leaving July 1st and need help in busy pediatric practice. Excellent salary leading to full partnership. Contact Charles Woods, M.D., 400 Stillson Road, Fairfield, Connecticut 06430.

CONNECTICUT-PSYCHIATRIC RESIDENCIES Geographically decentralized 1500-bed hospital. Approved 3-year program providing intensive training and experience with individual supervision in all psychiatric modalities. Visiting lecturers. Seminars. Associated with Yale University Department of Phychiatry and Neurology. All senior administrators and training director Board certified and on the faculty of Yale University. Stipends: First year, $10,694; Second year, $11,289; Third year, $13,020. Liberal benefits, including free hospitalization. Please send all particulars with first letter to Mehadin K. Arafeh, M.D., Supt. Connecticut Valley Hospital, Box 351, Middletown, Connecticut 06457.

CONNECTICUT-SENIOR PSYCHIATRISTS—in a 3-year accredited dynamic, decentralized community-oriented mental hospital. Affiliated with Yale University, Wesleyan University, and University of Connecticut. Excellent opportunities for professional growth and advancement. Salary commensurate with experience and training. Psychiatrist I, $19,303; Psychiatrist II, $20,128; Psychiatrist III, $21,911. Liberal benefits. Eligibility for Connecticut license required. Send all particulars in first letter, including references, to Mehadin K. Arafeh, M.D., Superintendent, Connecticut Valley Hospital, Box 351, Middletown, Connecticut 06457.

EMERGENCY ROOM—Full-time preferred in 250 bed Bristol Hospital. General Practitioner or specialist. To join 3 full-time plus part-time physicians rendering 24 hour medical coverage to 55,000 community. Excellent, new facilities, nursing and specialty backup. Salary plus liberal benefits for full-time. Call or write Richard P. Fredericks, Administrator, Bristol Hospital, Brewster Road, Bristol, Connecticut 06010. Telephone 589-2000.

IDEAL OPPORTUNITY—for any professional desirable of choice location for offices. Main Street, first floor. Three separate rooms completely air conditioned. Panelling throughout, one room installed with wall-to-wall rug. Two individual wash rooms. Ample free parking. Sufficient lighting, heat, and hot water.

VACANCY FOR A PART-TIME PHYSICIAN—to serve as District Medical Consultant in Putnam. Duties involve essentially reviewing medical report, ascertaining disabilities, and advising vocational counselors in related medical matters. Connecticut license required. One hour per week. Job would be particularly interesting to physicians who are phasing out current private practice. For further information, please contact Mr. Clay White, District Supervisor, Connecticut State Division of Vocational Rehabilitation, Norwich District Office, 257 Main Street, Norwich. Telephone 887-3546.

PATHOLOGIST—part time for the Masonic Home and Hospital, Wallingford, Connecticut. Attractive, well paying, steady and not much time consuming position.

WANTED—Third man for Family Practice, no investment, salary if desired, equal time off, new 120-bed hospital next to office, Northern Connecticut, 15 miles from Hartford. J. Kristan and L. O'Connor, M.D., 57 Union Street, Rockville, Connecticut 06066.

OPENING FOR INTERNIST in 496 bed State Veterans Hospital—$21,911-$26,729—plus 6% adjustment October 1970. Many fringe benefits. Write or call Personnel Officer, Veterans Home and Hospital, Rocky Hill, Connecticut, 529-2571, Extension 395.

PHYSICIAN—part time; to work mornings in the office only. Practice limited to general medicine and aviation medicine. For further information contact, James E. Crane, M.D., 965 Hope Street, Stamford, Connecticut.

PSYCHIATRIC RESIDENT, PHYSICIANS, PSYCHIATRISTS—positions available at Norwich Hospital. Community oriented, geographically unitized hospital wth mainy forward-looking, exciting programs. Fully approved for three years psychiatric residency training with NIMH grants available. Resident's salaries begin at $10,690 and all salaries will be increased by 6% in October, 1970. Many fringe benefits. Write Superintendent, Norwich Hospital, Norwich, Connecticut 06360.

OBSTETRICS & GYNECOLOGIST—Third man needed, board-eligible or certified, with military obligations completed, to join two other physicians in Middletown. Starting salary $18,000; partnership after three years. Congenial stall, University town. Prospective applicants are encouraged to write to Donald E. Miller, M.D., 18 Crescent Street, Middletown, Connecticut.

OFFICE-HOUSE for sale. Connecticut shoreline area. Seven room office fully equipped—x-ray and lab. Excellent opportunity for immediate income from active, lucrative, practice. Close proximity to Yale-New Haven Medical Center. Physician recently deceased. For details write to: P.O. Box 222, Clinton, Connecticut 06413.

ANYONE INTERESTED IN THE ABOVE IS ASKED TO CONTACT THE EXECUTIVE DIRECTOR'S OFFICE, 160 ST. RONAN STREET, NEW HAVEN, CONNECTICUT 06511.

In Memoriam

Borkowski, Boleslaus Joseph, Bristol, Georgetown Medical College, 1928. Dr. Borkowski was a general practitioner in the Bristol area since 1929. He served on the staff of St. Francis' Hospital in Hartford and Bristol Hospital. Dr. Borkowski was a member of the Hartford County Medical Association, Connecticut State Medical Society, and the American Medical Association. Dr. Borkowski died May 2nd, at the age of 69.

Calef, Bension, Elmwood, St. Louis Medical School, 1932. Dr. Calef was an internist in the Hartford area since 1946. He was on the staffs of Mt. Sinai, St. Francis and Hartford Hospitals. Dr. Calef was a member of the Hartford County Medical Society, and the Connecticut State Medical Society. Dr. Calef died May 11th, at the age of 62.

Jones, Robcliff Vesey, Stamford, Columbia Physicians & Surgeons, 1946. Dr. Flanagan specialized in Physical Medicine and Rehabilitation since 1956. Dr. Jones served in the U.S. Army, World War II, 1947-1949. He was on the staff of Yale-New Haven Hospital. Dr. Jones was a member of the Fairfield County Medical Association, Connecticut State Medical Society, and the American Medical Society. Dr. Jones died May 19th, at the age of 48.

Sturtevant, James Melvin, North Stonington, Bowdoin Medical School 1914. Dr. Sturtevant was a pediatrician in the New London area since 1941. Dr. Sturtevant served as a Captain in the U.S. Army Medical Corps in France, during World War I. He was on the staff of the Lawrence-Memorial Hospital. Dr. Sturtevant was a member of the New London County Medical Association, Connecticut State Medical Society, and the American Medical Society. Dr. Sturtevant died April 19th at the age of 83.

Anesthesiology Grand Rounds
Yale-New Haven Hospital
The Endotracheal Tube Could Not Be Removed

Romulo L. Villar, M.D., Jakub Goldstein, M.D.,
Samuel M. Lerner, M.D. and Frederick W. Hehre, M.D.

Dr. Jakub Goldstein:

A 63 year old female who qualified as 'Queen of the Weightwatchers" by losing over 100 pounds in less than 1 year from an initial weight of 270 lbs., was admitted for abdominal hysterectomy.

The patient stated that she had suffered cardiac arrest during previous breast surgery elsewhere. In 1967 she had an uneventful left nephrectomy for chronic pyelonephritis in Yale-New Haven Hospital. Past history included treatment for hypertensive cardiovascular disease, peptic ulcer and diverticulitis. Physical examination revealed a short, obese female whose blood pressure was 180/90 mm Hg. She exhibited a grade I systolic murmur at the cardiac apex and minimal ankle edema. Pelvic examination showed uterine fibroids and an ovarian tumor mass. Laboratory data: Hematocrit 39%; EKG: within normal limits. Gastrointestinal series, cholecystography and intravenous pyelography were interpreted as normal. Urine culture showed 4 + E coli.

Anesthesia was induced with thiopental 150 mg. and maintained with halothane and nitrous oxide. Succinylcholine 80 mg. was used to facilitate endotracheal intubation with #36 Murphy tube; the cuff was not inflated. A total of 36 mg. of curare was administered during the surgical procedure which lasted 2 hours 40 minutes. In view of her obesity and history of cardiac arrest, it was decided to support her ventilation post-operatively, therefore, the endotracheal tube was left in place and the curare was not reversed.

In the Recovery Room, the cuff was inflated by an inhalation therapist to prevent air leak around the tube. Thirty minutes later, the patient was awake and breathing adequately. An attempt at extubation failed. The endotracheal tube could not be removed. Direct laryngoscopy revealed no reason for the obstruction. Radiographic examination of the neck demonstrated the tube within the trachea, but the cuff was not visualized. Bronchoscopy through the endotracheal tube revealed no abnormality. The trachea was anesthetized with transtracheal tetracaine 10 mg., and the cuff deliberately needled. The patient was prepared for tracheostomy, and with a surgeon scrubbed and gowned, the tube was forcibly removed. The cuff was deflated, but at its distal end a ring of cuff had formed which was the apparent cause of difficulty. (Fig. 1) The patient was placed in a high humidity oxygen tent and given hydrocortisone 100 mg. every 4 hours for 24 hours. The patient was hoarse but this improved gradually over the next week. She did not exhibit stridor, retraction or shortness of breath, and, remained afebrile. Indirect laryngo-

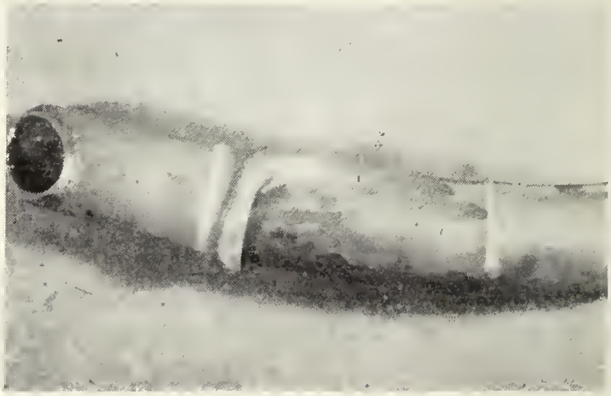

Figure 1

Endotracheal tube after extubation showing the ridge of the cuff.

DR. ROMULO L. VILLAR, Attending Anesthesiologist, Yale-New Haven Hospital, New Haven, Conn.

DR. JAKUB GOLDSTEIN, Attending Anesthesiologist, Yale-New Haven Hospital, New Haven, Conn.

DR. SAMUEL M. LERNER, Attending Anesthesiologist, Yale-New Haven Hospital, New Haven, Conn.

DR. FREDERICK W. HEHRE, Attending Anesthesiologist and Associate Director of Anesthesiology, New Haven, Conn.

From the Division of Anesthesiology Yale University School of Medicine and the Department of Anesthesiology Yale-New Haven Hospital, New Haven, Connecticut.

scopy 10 days later revealed no pathology, and she was asymptomatic on discharge.

Dr. Romulo Villar: May I briefly review the pertinent anatomy of the larynx?

The larynx is made up of cartilage, muscles, ligaments and membranes forming an inverted pyramidal tube bounded by the hyoid bone superiorly and the trachea inferiorly. It lies in the midline of the neck between C4 and C6, bounded anteriorly by skin and deep cervical fascia, laterally by the strap muscles and inferior constrictor of the pharynx and posteriorly by the hypopharynx.

The skeleton of the larynx is made up of nine cartilages—three paired and three unpaired. (Fig. 2) The unpaired cartilages are: The epiglottis—shaped like a leaf; the thyroid cartilage—shaped like a shield; and, the cricoid cartilage—shaped like a signet ring. The cricoid is the only cartilage of the laryngeal skeleton which forms a complete ring. It expands into a broad lamina posteriorly and is narrow anteriorly. On the top of the broad lamina and on each side, are the articular facets for the arytenoid cartilages.

The three paired cartilages are the arytenoids, the corniculates and the cuneiforms. The arytenoids are pyramidal in shape with the apex superiorly upon which the corniculate cartilages are placed. The arytenoid base has an anterior projection, the vocal process, to which the vocal ligament is attached, and, a broad lateral projection, the muscular process, for insertion of the crico-arytenoid muscles.

The quadrangular membrane and the conus elasticus form the elastic membranes of the larynx. (Fig. 3) The upper part of the conus elasticus forms the true vocal cords. The lower part of the quadrangular membrane forms the false vocal cords. Between is a space called the laryngeal sinus, or ventricle.

The mucosa of the upper respiratory tract is lined with ciliated pseudostratified columnar epithelium, except over the vocal cords which are covered with squamous epithelium.

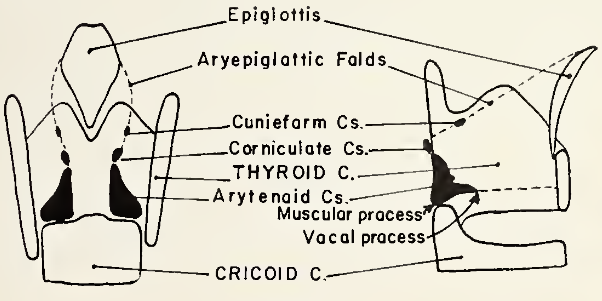

Figure 2
The skeleton of the larynx showing the upaired cartilages in white and the paired cartilages in black.

Discussion

Dr. James I. Gilman: How far below the cords was the cuff estimated to be? You cannot visualize it on this X-ray.

Dr. Robert Hook: The top of the cuff was one centimeter below the cords, because it could just be seen by direct laryngoscopy.

Dr. Gilman: Then the lower end of the cuff, which is roughly 2.5 centimeters long, was caught at the cricoid ring. Tracheal rings are horseshoe shaped, open posteriorly, and not circumferential. The only complete ring is the cricoid. You can enlarge and dilate a normal trachea by pressure, but not the cricoid ring.

Dr. Hook: The tube wouldn't budge a millimeter. I agree the fold was at the level of the cricoid.

Dr. Gilman: When it was removed, did this lip actually extend all the way around?

Dr. Frederick W. Hehre: Yes. It dried for a couple of hours before this picture was taken. (Fig. 1)

Dr. Gilman: If it was caught at the vocal cords, the cuff would have been visible the full length of the epiglottis, and would have been visible in the hypopharynx. We have trouble getting endotracheal tubes in. People remove tubes inadvertantly. This is the first one I have ever heard of that could not be removed.

Dr. Hehre: I would like to emphasize the main point in presenting this case, which is, what do you do when you are faced with this sudden happening? How best to protect the patient? You should say "stop", but the tendency is always to give a stronger pull. Having stopped, how do we investigate? This tube could neither be pushed in nor pulled out. Trauma could be produced by forcing it. The first thing must be to assure a patent airway. She was breathing; she was not comfortable, and, she was frightened. We reassured her, laryngoscoped her, and X-rayed her neck. We were unable to determine anything in relation to the cuff. We were not

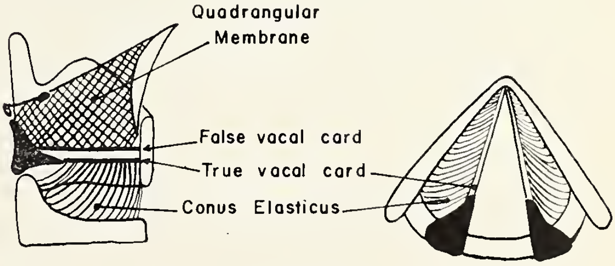

Figure 3
The elastic membranes of the larynx.

sure whether the cuff had been deflated so we deliberately deflated it transtracheally with a needle. We still couldn't budge the tube.

Eventually we would have to remove it, but we had to be ready to perform an emergency tracheotomy. We didn't know whether the cuff had slipped or whether there was something intrinsically wrong in the tube. An infant bronchoscope was inserted through the tube. A straight cystoscope could have been used, too. This showed nothing. We were faced with extubation because we could not make any further diagnosis, but we had to be ready to re-establish an airway immediately. The surgeon was scrubbed, gowned, gloved, and the tracheostomy set was open. The local anesthetic was even injected into her neck. Everything was ready. Thought and preparation of each step to insure the patient's safety must precede each definitive act.

Dr. Gilman: One cannot emphasize strongly enough about being prepared when you see the complication coming. Usually, we don't. This problem was in front of you.

Dr. Hehre: The cuff was not inflated initially and one wonders how much the cuff material expanded as it assumed body temperature. Obviously, enough to form the ridge.

Dr. Gilman: There was no leak with positive pressure ventilation during operation, so it was a snug fit. There may have been some laryngeal edema. Children, intubated for as little as 45 minutes, may exhibit sub-glottic edema after extubation. The areolar tissue beneath the mucous membrane swells quickly, and the most atraumatic intubation may produce edema. The worst place is within the cricoid ring. Any edematous expansion is inward until it closes the lumen.

Dr. Michael Chun: Should we put the biggest tube possible into the patient?

Dr. Gilman: No. A reasonably comfortable fit.

Dr. Hehre: It is how atraumatically the tube is introduced rather than the size of the tube.

Dr. Luke M. Kitahata: Could you inflate the cuff after she was extubated?

Dr. Hehre: No. It was broken with the transtracheal needle.

Dr. Kitahata: You did not inject contrast media to visualize the cuff?

Dr. Hehre: No.

Dr. Gilman: We have tried this. Radiopaque substances are oily and viscous, and it is almost impossible to get it down the catheter into the cuff. It does not spread out well inside the cuff either, unless you inject a large volume. We have seen portex tracheostomy tubes which have been difficult to remove after the cuff has been inflated for a long time at body temperature. The cuff loses its elasticity and stays enlarged, and is difficult to remove the tube and may start bleeding.

Probably the majority of discoveries in biology and medicine have been come upon unexpectedly or at least had an element of chance in them especially the most important and revolutionary ones.—*W. B. Beveridge. Quoted by M. B. Strauss in Familiar Medical Quotations.*

Special Article

Auditing of Physicians' Records

Arnold J. Streich, LL.B.

This is a study made at a request of the House of Delegates of the American Medical Association of the legality of on-site audits in physicians' offices, their permissible extent and nature, and how they affect the confidentiality of physicians' records on their patients.

The Social Security Act provides that the state or local government agency administering a medical assistance program using funds provided by the federal government must include in plans established for this purpose procedures for determining the quality of medical service being delivered or the capability of the provider for delivering high quality medical service. The Act also provides for agreements with every person or institution providing services under the state plan to keep such records as are necessary to disclose the extent of the services provided. These requirements may be reasonably interpreted as authorizing "on-site audits in physicians' offices" to determine quality and capability for delivery of medical service and to provide for inspection of the required records.

With regard to "confidentiality of physicians' records," the Act requires the state plan to provide safeguards which restrict the use or disclosure of information concerning applicants and recipients to purposes diretly connected with the administration of the plan.

The authority of a state or local administrative agency to prescribe rules and regulations for administration of the law is well established. Investigatory or inquisitorial powers, power to inspect, or to secure or to require the disclosure of information by means of accounts, records, reports, statements, testimony of witnesses, production of documents, or otherwise are conferred on practically all administrative agencies, and these powers may be implied as well as expressed.

Among these powers is the power, for specific purposes, to enter premises and inspect or examine such premises or things or operations therein, particularly books and records. Some statutes authorize administrative agencies to enter and inspect such places and such records as they may deem necessary or appropriate to determine whether any person has violated any provision of the act being administered or which may aid in the enforcement of the act. However, such powers are not unbounded but are exclusively derived from and limited by the authorizing statutes.

Benefits under Title XIX of the Social Security Act are limited to those persons who specifically qualify under the terms of the Act. This serves to limit the extent of the "on-site audits" to records of medicaid recipients. While an examination of medicaid and nonmedicaid patients' records might not be beyond the scope of an inspection to determine the quality of medical services generally, it would be beyond the express or implied statutory authority to insist on the right to inspect the records of patients who have neither applied for nor are receiving medicaid.

An administrative body or official may be clothed with the authority to say when a law shall operate, or as to whom, or upon what occasion, provided the standards prescribed for guidance are as reasonably precise as the subject matter requires or permits. Statutes, ordinances or regulations which give an administrative agency an absolute, unregulated, and undefined discretion grant arbitrary powers and represent an unlawful delegation of legislative powers. The presumption that an administrative official will not act arbitrarily but will exercise sound judgment and good faith cannot sustain a delegation of unregulated discretion. The legislature cannot vest in an administrative agency the power, in its absolute or unguided discretion, to apply or withhold the application of the law or to say to whom a law shall or shall not be applicable.

The general rule, which requires an express standard to guide the exercise of discretion, is also subject to the exception that where it is impracticable to lay down a definite comprehensive rule, it is not essential that a specific prescribed standard

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ARNOLD J. STREICH, LL.B., Director, Corporate Law Department Legal Division, American Medical Association.

be expressly stated in the legislation. In such situations the courts will infer that the standard of reasonableness is to be applied.

It is not necessary that the legislature supply administrative officials with a specific formula for their guidance in a field where flexibility and the adaption of the legislative policy to infinitely variable conditions constitute the essence of the program.

It is a breach of professional ethics for the physician to reveal the confidential communications of his patients without the express consent of the patient, unless required by law.

Insofar as office audits of medicaid patients' records are concerned the right of the government to see to the application of public funds through the inspection of records is imposed as a condition both on the provider of the medical services and the medicaid recipient. In this situation the physician is doubly protected since he is required to open his records pursuant to law and a patient's authorization to do so may reasonably be implied since his right to receive benefits is subject to the same condition.

The same compulsion of law does not apply to records of non-medicaid patients. Where such patients are concerned, the physician would be acting within his rights in refusing to make his records available for inspection without the express consent of his patients. Administrative rules and regulations which require disclosure under these circumstances could be opposed on the grounds that they are arbitrary and in excess of delegated authority.

POSTGRADUATE COURSE IN LARYNGOLOGY AND BRONCHOESOPHAGOLOGY

November 9 through 20, 1970

The Department of Otolarynogology of the University of Illinois at the Medical Center will conduct a postgraduate course in Larynogology and Bronchoesophagology from November 9 through 20, 1970. This course is limited to fifteen physicians and will be under the direction of Paul H. Holinger, M.D. It will be held largely at the Eye and Ear Infirmary of the University of Illinois Hospital, 1855 West Taylor Street, Chicago, and will include visits to a number of other Chicago hospitals. Instruction will be provided by means of animal demonstrations and practice in bronchoscopy and esophagoscopy, diagnostic and surgical clinics, as well as didactic lectures and several motion pictures.

Interested registrants will please write directly to the Department of Otolaryngology, Abraham Lincoln School of Medicine of the College of Medicine, University of Illinois at the Medical Center, Postoffice Box 6998, Chicago, Illinois 60680.

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1. Kannel, W.B., *et al.*: *Circulation* 35:734, 1967.
2. Thomas, H.E., Jr., *et al.*: *Med. Times* 95:1099, 1967.
3. Albrink, M.J., in: Beeson, P.B. & McDermott, W. (eds.): *Cecil-Loeb Textbook of Medicine*, ed. 12, Phila.: W.B. Saunders Co., 1967.

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X-Ray of the Month

Section of Chest Diseases

Yale-New Haven Medical Center

Arnold B. Rilance, M.D., Director, Winchester Chest Clinics

History

M.E. #70-18-91. 2nd. admission of an 18 year old single female. The patient was completely asymptomatic until 11:25 A.M. on 5/19/69 when, while sitting in class at school, she suddenly developed pain in the region of the right scapula. It was constant in nature, aggravated by motion of the right shoulder girdle. It was also aggravated by deep breathing. The patient was seen in the E.R. and subsequently admitted to the hospital. The patient had been on birth control pills since December, 1967. There was no history of a similar prior episode of pain. She denied hemoptysis, calf pain and pelvic pain. There was no history of fever, night sweats, palpitation or pain in the anterior chest; no history of peripheral lymphadenopathy or skin rash; no history of weight loss. The patient ran a low grade fever for the first ten days.

Systemic Review

Otherwise negative.

Physical Examination

Revealed diminished breath sounds over the right posterior chest with an inconstant friction rub. Occasional rhonchi were heard over the right upper lobe.

Laboratory Tests

Normal WBC and differential. A variety of blood chemistries, serum proteins and serum enzymes were normal. Sputum cytology was negative x 3. Tuberculin and cocciodin skin tests were both negative. A bone marrow examination was normal.

Special Studies

Laminagrams of the chest revealed a right-sided hilar mass.

Lung scan: demonstrated decreased uptake in upper ½ of the right lung field.

Pulmonary angiogram: Pulmonary artery pressure—20 mm. Hg. The left lung circulation was normal. The right main pulmonary artery was dis-

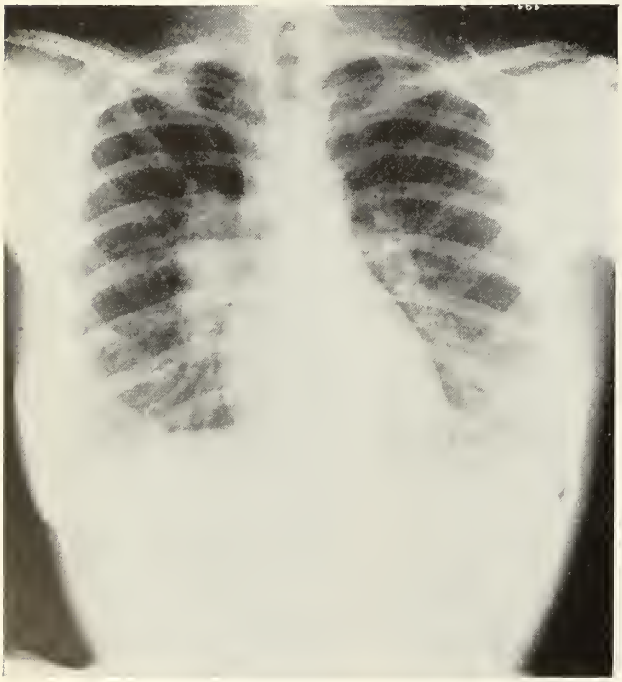


Figure 1
Admission chest X-ray demonstrating marked enlargement of right hilum due to adenopathy.

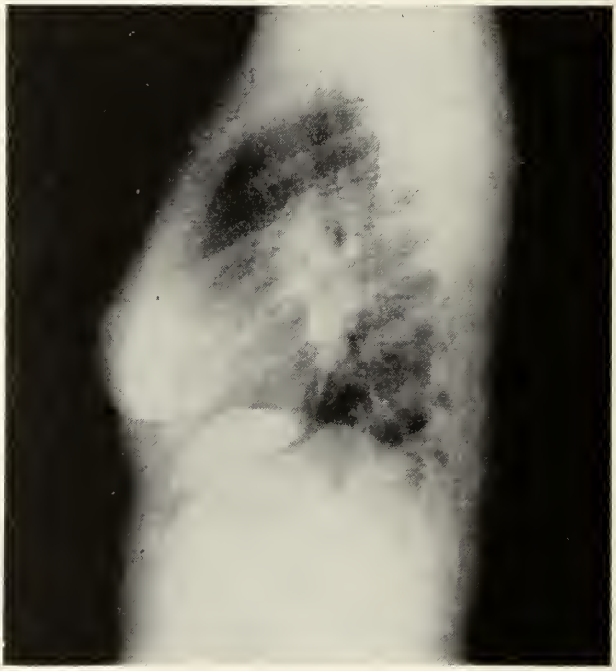


Figure 2
Lateral view demonstrates gross enlargement of hilar shadow most compatible with lymphadenopathy.

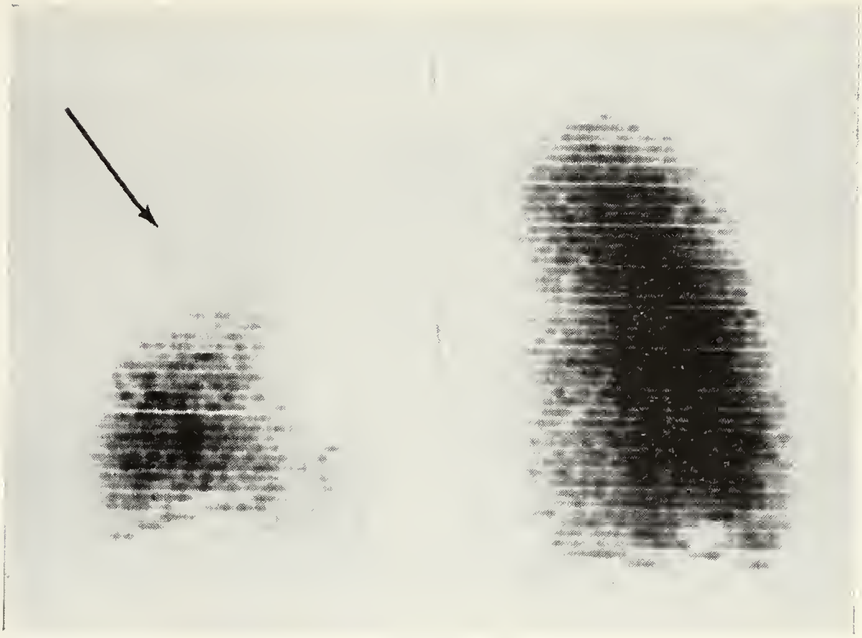


Figure 3

Photograph of lung scan demonstrating (arrow) almost complete absence of perfusion in right upper lobe.

placed laterally and superiorly and shows encroachment along its inferior aspect by enlarged nodes. The entire right lung is underperfused. There was marked narrowing and displacement of the right upper lobe artery probably due to external compression.

Scalene node biopsy: revealed many granulomata with giant cells and slight central necrosis.

Liver biopsy: revealed granulomata consistent with sarcoidosis.

IVP—normal.

Discussion

On admission the clinical impression was that of pulmonary embolism. Further studies revealed a large perfusion defect in the right upper lobe due to hilar adenopathy demonstrated to be due to sarcoidosis.

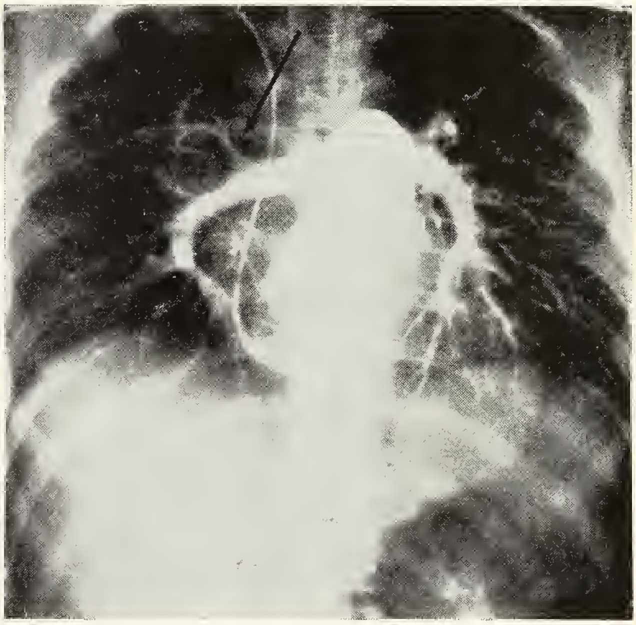


Figure 4

Pulmonary arteriogram demontrates displacement laterally of right main pulmonary artery with (arrow) marked stenosis of right upper lobe artery. Diminished arterial perfusion throughout right lung.

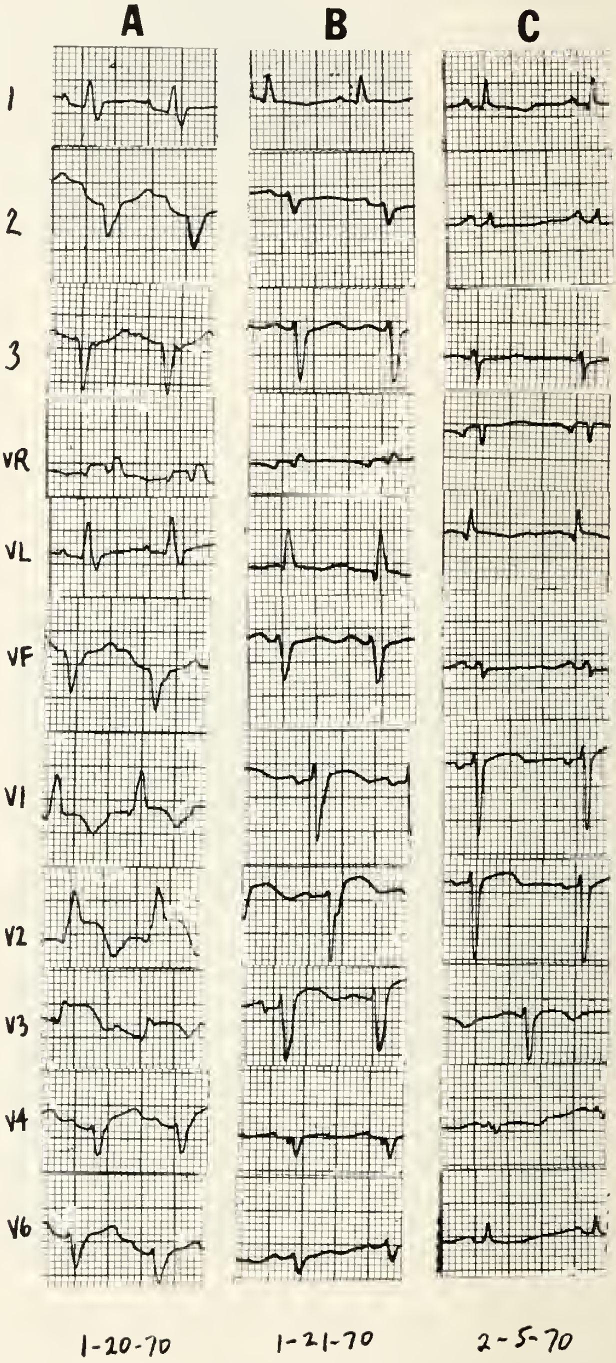
Electrocardiogram of the Month

Yale-New Haven Hospital
New Haven, Connecticut

Prepared by
HYMAN M. CHERNOFF, M.D.
Associate Professor of Clinical Medicine,
Yale School of Medicine
Director, Dept. of Electrocardiography
Memorial Unit, Yale-New Haven Hospital

It is not uncommon, particularly following acute occlusion of the left coronary artery, to observe the development of varying degrees of impaired conduction in the bundle system in one or in both ventricles. Since the main blood supply to the right bundle branch and to the anterior (superior) division of the left bundle branch usually arises from a branch of the anterior descending branch of the left coronary artery, infarction of the anterior wall is often followed by the development of either right bundle branch block alone, or left anterior hemiblock alone, or by a combination of right bundle branch block and left anterior hemiblock. When both right bundle branch block and left anterior hemiblock occur the only pathway by which an atrial impulse may reach the ventricles is via the posterior (inferior) division of the left bundle. Any further extension of the pathologic process to involve this division will therefore result in the development of complete heart block. This is reflected in a rather high incidence of sudden cardiac arrest in patients in whom right bundle branch block and left anterior hemiblock develop acutely after an anterior wall infarct. This has led some physicians to recommend prophylactic insertion in such patients of an artificial demand pacer to take over control of the ventricles should arrest occur. Recent studies, however, suggest that this does not significantly reduce the mortality rate is such patients. Moreover, as illustrated below, the impairment in conduction in the various branches of the bundle system may be transient and subside spontaneously.

In the electrocardiogram the development of impaired conduction limited only to the anterior division of the left bundle can be recognized by a marked leftward shift in the mean frontal QRS axis, usually to the range of minus 60 degrees. The QRS interval may increase slightly but does not reach a 0.12 sec. duration. The combined presence of right bundle branch block and left anterior



hemiblock is recognized in the electrocardiogram by the finding in the chest leads of patterns typical of right bundle branch block and of abnormal left axis deviation in the limb leads.

Tracing A, taken on 1-20-70, 24 hours after onset of pain, reveals ST segment elevation and abnormal Q-waves in leads V1, V2, and V3 consistent with recent infarction of the anterior septal area. In the chest leads the I-V conduction time is prolonged to 0.12 sec., and the patterns of QRS are consistent with the presence of right bundle branch block. In the limb leads there is abnormal left axis deviation to about minus 60 degrees, consistent with impaired conduction in the anterior division of the left bundle branch.

Tracing B, taken on 1-21-70 reveals subsidence of the patterns of right bundle branch block in the chest leads. The I-V conduction time has shortened to about 0.09-0.10 sec. However, abnormal left axis deviation of about minus 60 degrees persists in the limb leads, consistent with persistence of the left anterior hemiblock.

Tracing C, taken on 2-5-70 reveals shortening of the I-V conduction time to about 0.08 sec. The mean frontal QRS axis is now within normal limits at about plus 20 degrees. These findings are consistent with subsidence of the left anterior hemiblock. The poor progression of the R-waves in the chest leads and the presence of Q-waves and abnormal T-waves in leads 1 and aVL are consistent with the evolved pattern of anterior wall infarction.

Symposium On Industrial Rehabilitation

Wednesday, July 29th

A "Symposium on Industrial Rehabilitation" under the auspices of Waterbury Hospital; Department of Physical Medicine and Rehabilitation will be held on Wednesday, July 29th, at Merriman Hall (School of Nursing), Waterbury Hospital.

The program for the one-day symposium will begin with registration at 9:00 a.m. and will feature some of the leading people in various aspects of rehabilitation.

E. R. Tichauer, professor and director of the Division of Biomechanics, N.Y.U. Institute of Rehabilitation Medicine and consultant in biomechanics for Waterbury Hospital, will speak on *"Biomechanics Applied to the Development of Work Tolerance in Industrial Rehabilitation"*.

Mrs. Gregory Lynch, compensation commissioner with the State of Connecticut will discuss *"Compensation Laws"*.

Luncheon speaker will be Dr. Morris Granoff, president of the Connecticut State Medical Society. His talk will be on *"The Role of the Industrial Physician in Rehabilitation"*.

Dr. Murray Freed, professor and chairman of the Department of Rehabilitation Medicine, Boston University School of Medicine will discuss *"Rehabilitation of Spinal Cord Injuries"*.

"Federal and State Vocational Rehabilitation Services" will be the subject of a talk by Mr. Joseph Marra, chief of the Bureau of Rehabilitation Services, Connecticut State Division of Vocational Rehabilitation.

NEW BOOKS IN REVIEW

MASTERING YOUR EMOTIONS: MENTAL HEALTH THROUGH THE REEDUCATION OF SELF. Edited by William B. Terhune, M.D. William Morrow & Company, Inc., New York, 1970 249 pp. $5.95.

Reviewed by: LOUIS H. NAHUM

What the author has to teach in this book is re-education as a way for people to profit in mastering their emotions. It is in one sense a philosophy of life and in another sense a practical approach to human improvement which the author states he has successfully used over the years in treating patients at Silver Hill Terhune Clinic in New Canaan, Conn.

Re-education approach to emotional difficulties really began in 1890 by Dr. Paul DuBois in Switzerland, was then successfully employed in France and in this country at Austin F. Riggs Institute in Stockbridge, Mass. where the author first learned to use the method.

The theory behind Re-education is simply this: just as an individual can be physically retrained in new habits of walking or talking, so he can be retrained in new habits of thinking, feeling and acting. The method, however, can only be an adjunct to both psychiatry and neurology. The psychiatrist knows when the method should be applied as well as those mental disorders in which other techniques will be more efficacious.

Re-education appears to succeed best in common functional disorders that plague many of us such as psychosomatic disturbances, hypochondriasis, chronic anxiety states, mild depressions, ineffectiveness, chronic sour dispositions, the projectors, eating disturbances, marital difficulties, social and work problems, aging, and intemperance.

Re-education the author claims activates the intelligence, retrains emotions and stresses physical improvement by emphasizing intelligence, need for understanding self and others, need to face reality, self-discipline. Apparently it seeks to teach practical idealism and culminates when successful in personal mental hygiene.

There are 12 chapters all full of common sense, wisdom and encouragement to make something of yourself. The last chapter is a technique of self inventory which permits a person to follow his own progress from month to month and year year.

The person who realizes his weakness and wants to be better will find support in this book.

DUNCAN'S DISEASES OF METABOLISM. Sixth Edition. Edited by Philip K. Bondy (in association with Leon E. Rosenberg). Volume I, xx + 710 + xxvii + 12 pages; Volume II, xv + 667 + xxvii + 11 pages. W. B. Saunders Company, Philadelphia, 1969. $39.00.

Reviewed by: JOSEPH S. FRUTON

Since the appearance in 1942 of the first edition of Garfield Duncan's collective treatise, each successive revision of this famous work has been obliged to take account of the explosive development of biochemistry during the past quarter-century. This is especially true of the present edition, and the editors and authors have clearly made a strenuous effort to include all recent developments relevant to the topics under discussion. Indeed, at the end of each volume is an appendix in which the main text is brought up to date (as of 1969).

This work involved the collaboration of 34 contributors, and despite this multiplicity of authorship, the two volumes have a unity of structure that is impressive. This arises in large part from the editor's plan to divide the text into four major sections: Genetics, Intermediary Metabolism, Metabolic Regulators, and Nutritional Factors. The first section is relatively brief, and includes chapters on Gene Structure and Function (Weissman and Brawerman), Inborn Errors of Metabolism (Rosenberg), and Molecular Diseases (Konigsberg). These chapters provide a succinct introduction to current views on the role of DNA and RNA in the translation of the genetic message into the structure of proteins. The largest section of the treatise, devoted to Intermediary Metabolism, includes outstanding reviews on Metabolic Interrelationships between Carbohydrates, Lipids, and Proteins (Coleman), Disorders of Carbohydrate Metabolism (Bondy), Diseases of Lipid Metabolism (Scheig), The Sphingolipodystrophies (Brady), Disorders of Amino Acid Metabolism (Rosenberg and Scriver), Diseases of Purine and Pyrimidine Metabolism (Seegmiller), Porphyrin Metabolism and the Porphyrias (Tschudy), Disorders of Bilirubin Metabolism (Berlin, Berk, and Howe), and Disorders of Connective Tissues (Bornstein).

The second volume contains, in the section on Metabolic Regulators, excellent chapters on Neuroendocrine Interrelations (Guillemin), The Anterior Pituitary Gland (Ney), Disease of the Thyroid (Rawson, Money, and Greif), The Adrenal Cortex (Bondy), The Adrenal Medulla and Catecholamines (Levine), Parathyroid Hormone, Thyrocalcitonin, Vitamin D, Bone and Bone Mineral Metabolism (Potts and Deftos), Aldosterone in Hypertension and Edema (Mulrow), Water Metabolism and the Neurohypophysial Hormones (Kleemand and Vorherr), Acid-Base Balance (Levitin), The Testis (Lipsett), The Ovary (Kase), and Nonendocrine Secreting Tumors (Amatruda). The final section, on Nutritional Factors, contains chapters on Undernutrition (McLaren), Overnutrition and the Fat Cell (Albrink). The Vitamins (McLaren), and Metabolism of Trace Metals (Scheinberg and Sternlieb). Each of the chapters has a valuable list of references, and both volumes contain the index to the entire work. The printing of the text, diagrams, and ilustrations is of good quality.

Inevitably, in a collective work of this kind, there is some unevenness of style and clarity of exposition. On the whole, however, the individual chapters are well-written, and a thoughtful editorial supervision is evident. This reviewer found remarkably few errors in the sections covering material with which he was familiar; no doubt most of them will be corrected in subsequent printings. All the people associated with the writing of this book, and especially Doctors Bondy and Rosenberg, are to be congratulated on having provided the most complete and up-to-date reference work available at present on the biochemical factors in human disease.

LAW—MEDICINE NOTES

J. Alfred Fabro, M.D.

Anatomy Of A Case

Editor's note: This is an actual case with identifying names deleted. It is instructive as the principles enuciated are applicable to the responsibilities and liabilities of physicians in prescribing drugs. For example, one could well substitute one of the birth control drugs, especially if a patient has not been instructed in the complications or dangers of use of the drug. The case was settled in favor of the plaintiff.

Mr. P., Administrator of Estate of
Mrs. P., deceased—Plaintiff
vs
Dr. S., Defendant

PLAINTIFF'S TRIAL MEMORANDUM

I. Statement of Facts

This is a medical malpractice and products liability case against a doctor, involving alleged negligence and breach of warranty. Plaintiff sues for damages under the New Jersey Survivors' Action for personal injuries to plaintiff's decedent, and under the New Jersey Wrongful Death Act for pecuniary loss suffered by plaintiff's decedent's next of kin.

Plaintiff's decedent, Mrs. P., was born on October 18, 1924, and was 40 years of age at the time of her death on March, 1965. She devoted her full time as housewife and mother.

During November, 1964, Mrs. P. suffered from a severe cold, and consulted her family physician, Dr. L. He treated her for a bronchitis from November 5, 1964 until December 3, 1964.

Thereafter, she consulted the defendant Dr. S., who examined her for the first time on December 8, 1964 at his office. Dr. S. referred Mrs. P. to a laboratory for sensitivity and sputum culture tests, and on receipt of the results, prescribed for her a drug called chloromycetin.

Dr. S. diagnosed her condition on his initial examination as "slow resolving pneumonia left lung," which he finally diagnosed as "bacterial pneumonia, mixed type."

Dr. S. also arranged to have her X-rayed, and the radiologist reported to him that she had a "resolving pneumonia process" in her left lung.

The defendant Dr. S. examined Mrs. P. on December 8, 1964 and on December 21, 1964, and prescribed chloromycetin on December 12, 1964, December 21, 1964, and December 28, 1964. The refill of the prescription was ordered by telephone on December 28, 1964, without Dr. S. having physically examined Mrs. P. on the said date.

Dr. S. has admitted in pretrial discovery that he was aware that prior to prescribing chloromycetin for Mrs. P. he was familiar with the medical literature pertaining to the side effects of chloromycetin, among which was listed aplastic anemia. Dr. S. never contacted Dr. L. during the time he prescribed the said chloromycetin, nor did he arrange for any blood studies to be taken, although he was aware that the manufacturer had recommended that blood studies be taken during the time chloromycetin is prescribed.

When Mrs. P. last saw Dr. S., he advised her that her lungs had cleared up, and that everything would be all right, and that it would not be necessary for her to come back.

Early in February 1965 Mrs. P.'s husband noticed some small bumps on the lower part of her legs. Blood blisters were also appearing in her mouth. Mr. P. spoke to Dr. S. concerning the blood blisters in her mouth and the marks on her body, and Dr. S. advised him that his wife was probably suffering from emotional disturbances, and prescribed some medication for her nerves.

Mr. P. decided to take his wife back to Dr. L., and saw him on March 1, 1965. Dr. L. arranged to put Mrs. P. in a hospital, where she was hospitalized from March 1, 1965 until her death on March 5, 1965. The cause of death has been set forth as aplastic anemia following the administration of chloramphenicol (chloromycetin).

II. Factual Contentions as to Defendant's Liability

A., As To Dr. S.

Plaintiff contends that the defendant Dr. S. was negligent and careless in the following respects:

DR. J. ALFRED FABRO, Senior Attending Surgical Staff of the Charlotte Hungerford Hospital, Torrington, Conn.

1. In prescribing the drug chloromycetin for plaintiff's decedent when her physical condition did not justify same.

2. In failing to warn the decedent and the plaintiff concerning the dangers of the said drug, and the known side effects.

3. In failing to follow the recommendations of the manufacturer of the said drug with regard to precautions to be taken in prescribing same.

4. In failing to take blood studies and bone marrow studies of the decedent during the time she was taking the said drug.

5. In failing to render proper medical advice to the plaintiff, when he was informed of the decedent's complaints.

6. In failing to consult with Dr. L., who had previously treated plaintiff's decedent.

7. In failing to make proper observations of the decedent during the time he prescribed the said drug.

8. In failing to require the decedent to report to him more frequently during the time she was taking the said drug in order to observe the effects of same.

9. In failing to follow the recognized standards and procedures of his professional calling with reference to the drug chloromycetin.

III. Legal Contentions as to Defendant's Liability

It is contended that the defendant Dr. S., as an expert in internal medicine, owed plaintiff's decedent the duty of exercising reasonable and prudent care commensurate with his specialized professional calling, and was required to keep abreast of the advance state of medical knowledge, particularly with what was known to the medical profession with respect to the indications and contraindications of the drug, chloromycetin.

It is contended that the defendant was negligent and careless in prescribing the said drug for the decedent's condition when same was contraindicated and less harmful drugs would have been adequate to treat her condition.

It is further contended that the defendant, after prescribing chloromycetin, failed to take proper blood studies which were recommended by the manufacturer in its package inserts, and also in the medical literature, including the Physicians Desk Reference, an authoritative source of information for doctors who prescribe drugs for the treatment of patients.

The duty of care owed by a physician[1] has been clearly set forth in a number of leading New Jersey cases. A physician is required to make proper and careful examination of the patient[2] to determine whether or not he is suffering from any side effects from a drug which he prescribes, and such failure to properly and carefully examine the patient constitutes negligence.

A physician is under an obligation to consult with other physicians for supplemental care, advice or treatment of a patient when the condition so indicates. In the instant case, the facts disclose that the defendant erroneously assumed that plaintiff's decedent had received blood studies from another physician. Although he knew that the decedent had previously been treated by Dr. L., he never attempted to contact Dr. L. to find out whether he was still treating the decedent and to inform him that he was prescribing chloromycetin.

Not only was his assumption erroneous, since the decedent was not going to Dr. L. at the time she submitted herself to the care of the defendant Dr. S.; but it would appear to be a matter of professional misconduct for one physician to treat the patient of another without notifying the patient's original physician that he was so doing. At the very least, the defendant Dr. S. owed a duty, not only as a professional courtesy, but from the standpoint of the patient's welfare, to consult with Dr. L. before endangering the health of the decedent by prescribing a drug known to be dangerous.

In this case, the defendant failed to take blood studies to determine whether or not the decedent showed any signs of blood dyscrasia which ultimately resulted in aplastic anemia from which she died.

In a cited case, the court[3] properly admitted a brochure of the manufacturer where the brochure contained warnings as to the use of the drugs, which the defendant doctor negligently failed to follow.

In a recent case[4] a physician was held to be negligent in prescribing chloromycetin for a patient without warning as to the possible or probable injurious effects from its use. The doctrine of "informed consent"[5] imposes a duty upon a physician to inform the patient of the nature and hazards of disease or treatment.

It is significant that the defendant admitted in pretrial discovery that he was aware that fatal cases of aplastic anemia followed the taking of the drug chloromycetin. The medical literature was replete with reported cases of aplastic anemia attributed to the taking of chloromyetin. Governmental inquiries were brought to the attention of physicians, warning of the hazards of prescribing chloromycetin when less harmful drugs were drugs of choice. In spite of this knowledge, the defendant Dr. S. prescribed chloromycetin without informing the decedent or her husband concerning possible side effects, and without making an effort to determine whether she developed blood dyscrasia by obtaining blood studies during the time he prescribed the said drug. As a matter of fact, the final prescription was given over the telephone, without even the benefit of a physical examination.

Defendant is not relieved from the duty to inform himself sufficiently from sources other than the manufacturer concerning the potential hazards and need for blood studies when he continued to prescribe the drug.

IV. Damages

Plaintiff seeks compensatory damages against Dr. S.

The action for compensatory damages is based both upon the New Jersey Wrongful Death Act and the New Jersey Survivor's Act. Under the New Jersey Wrongful Death Act, the plaintiff is entitled to damages based upon the pecuniary loss suffered by the decedent's next of kin. The sum recoverable is the present value of the pecuniary injury to the next of kin. In awarding damages to the husband and children of the deceased housewife and mother, a jury may consider the pecuniary value of services performed by the decedent, including keeping of the house, cooking, cleaning, caring for children, guidance, etc.

A home economist may be used as an expert to evaluate the loss of services of a housewife and project what the cost would be of a substitute mother and wife who would have to assume the role of cook, dishwasher, dietician, waitress, governess, baby sitter, laundress, dressmaker and general housekeeper.

In the case of the death of Mrs. P., she was 40 years of age, and had a life expectancy of 36.61 years at the time of her death, on March 5, 1965.

In awarding compensatory damages under the Survivor's Act, the jury should consider as a measure of damages that a debt was owed to plaintiff's decedent to compensate her estate for the pain and suffering undergone by her during her lifetime, which was due to the negligence of the defendants.

In addition, the General Administrator of her estate is entitled to recover for out-of-pocket expenses, including medical and hospital bills, as well as funeral expenses.

References

1. Carbone v. Warburton, 22 N.J. Super. 5, 91 A.2d 518 (App. Div. 1952).
2. Haring v. Banks, 7 N.J. Misc. 605, 146 A.675, aff. 106 N.J.L. 569, 150 A. 918 E. & A. 1930).
3. Marchese v. Monaco, 52 N.J. Super. 474 (App. Div. 1938).
4. Sharpe v. Pugh, 155 S.E. 2d 108 (Sup. Ct. N.C. 1967).
5. 79 A.L.R.2d 1028.

Letter To The Editor

Members of the Society are invited to communicate with the Editor expressing their opinions or giving information as to any matter of interest to the members. The Editorial Board reserves to itself the right to select the communications or excerpts therefrom that will be published and to reject others. As with other material which is submitted for publication, all letters will be subject to the usual editing. Address all correspondence to: THE EDITOR, CONNECTICUT MEDICINE, 160 St. Ronan Street, New Haven, Connecticut 06511.

Dear Doctor Nahum:

I want to commend you on the choice of topics you choose for your editorials particularly those pertaining to environment and population. It seems I have yet to see an issue of *Connecticut Medicine* that does not contain an editorial that is pertinent to the environment in one form or another. I suspect that this is one of your pet topics but nevertheless I feel you are fulfilling an important role in bringing these problems to the attention of the physicians of our state. It is unfortunate that on the State level, more has not been done both from an administrative and legislative standpoint as one would hope for. New York State is far ahead of us even at the present time and if the program of Governor Rockefeller as he gave his message to the legislature in January is carried out, New York State will be far ahead of Connecticut in having the mechanism of handling environmental problems.

I would also like to tell you how much I enjoy some of the other editorials you write that bear only slightly upon medicine. Articles on human behavior and sleep cycles have been particularly enjoyable.

Again, I thank you for presenting to us both interesting and enlightening material in the Journal.

Sincerely yours,
Paul A. Cooper, M.D.

Hartford, Conn.

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New Milford, Conn., Northwestern Conn. community hospital of 79 beds with planned expansion to 150 with ICCU. On Candlewood Lake, one hour from Long Island Sound, and one and one half hours from New York City. Rapid population growth, excellent schools, and skilled-level industry. Office space available. Medical Staff and hospital Board desires having the following physicians added to those already practicing in the area: Pediatricians, Internists, General Practioners, ENT, Obstetricians and Gynecologists. Further details will be sent by writing to: D. Randall Hays, M.D., Chief of Staff, New Milford Hospital, New Milford, Conn. 06776.

Effect Of Early Malnutrition On The Reaction Of Adult Rats To Aversive Stimuli

(*Nature*, 225, 468, Jan. 31, 1970) Levitsky, D. A., Barnes, R. H. A great deal of interest has been shown in the relationship between early malnutrition, especially protein-calorie malnutrition and intellectual capacity or learning ability. Early malnutrition may cause other changes in behavior such as motivation for food or water if it is deprived of them early in life.

Adult pigs which had been fed protein products early in life and then given a full diet took longer to extinguish a conditioned avoidance response than the controls.

In this communication the authors investigated whether a brief period of malnutrition very early in life increases the emotional reactivity of the adult to aversive stimuli. One effect of malnutrition during early development is to produce a rather long lasting, if not permanent, lowering of the threshold of the stress response system. Adrenals of early malnourished animals are consistently larger than in controls.

It is not yet clear whether early malnutrition results in deficient learning ability.—L.H.N.

WOMAN'S AUXILIARY

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PRESIDENT'S ANNUAL REPORT—1969-1970

Connecticut has completed another year of Auxiliary work with a feeling of accomplishment in some areas, but also realizing that a great potential lies untapped.

We have continued to support the Art Show, which is such an interesting part of this meeting time.

AMA-ERF contributions by the Auxiliary are up slightly over last year as this time.

Varied aspects of health and health education are covered by the Community Services committees, and an accurate report of all activities is difficult. Over the past few years the Auxiliary has encouraged the participation of its members in already existing health programs such as the distribution of hot meals to homebound invalids, bloodmobiles, and health fairs. Visual screening of the preschool child for amblyopia continues as one county's project, and another county has had several panel programs on the problems of today discussing drugs, alcohol, smoking, and sex education with participating physicians, lawyers, clergymen, and teachers.

Health Careers continues to be a very active committee of interest to almost every member. A Health Careers Reference Guide of Schools in Connecticut was distributed to high school counselors throughout the state in September 1969. A new book, Directory of Accredited Allied Medical Educational Programs 1960-70 has just been obtained and is being distributed, one to each county. As evidence of the great concern with health careers is the increase in the amount of money given in scholarships this year. The total amount awarded was $7,575 with $5,500 in medical scholarships, $1,375 in nursing, and $700 in other health career fields.

Mental health in Connecticut this year meant "learn about your mental hospital". Each county was urged to learn about the mental hospital which serves it, to understand its problems, and to offer assistance where possible. One county executive board held a meeting at its hospital, and was taken on a tour of its facilities. Another county entertained representatives of its hospital so as to increase the members' knowledge of the drug program at the hospital and how they could help them.

Something new came to Connecticut this spring—The Woman's Auxiliary to the Student American Medical Association. This group is made up of the wives of medical students, internes and residents in the Hartford area. The purposes of WA/SAMA are to provide sociability, service and educational programs of interest to these young women. WA/SAMA also helps with housing, and becoming acquainted when they move into a new area to take up an interneship or residency or settle in practice.

We wish to thank the medical society for granting us a booth among the scientific exhibits. We hope you will all take a moment at #41 to look at it and learn a little more about the Auxiliary. This is also a first for us and we hope both of us will benefit.

What's ahead for the Auxiliary? We need more participation in AMA-ERF, particularly in support of the two Connecticut medical schools. With the increased demands on all health services, health careers programs are a very important part of our work. The legislature will be in session next year, which always means a busy year for us. Health education demands never cease—sex education, drugs, alcohol, smoking, mental health. This education should be for both our members and the general public. With the costs of education rising each year our scholarships seem more important than ever. Public services such as bloodmobiles deserve continued Auxiliary support. So you can see, we never lack for programs of interest and need. It is important for us to enlarge our membership to increase the effectiveness of our organization.

Mrs. James F. Jones, *President*

AROUND THE STATE

NEW HAVEN COUNTY

Board of Governors

New Haven County Medical Association

May 28, 1970

The Board of Governors of the New Haven County Medical Association met on Thursday, May 28, 1970 at the Colonial House, in Hamden, under the leadership of President Stewart J. Petrie.

In order to improve communications between local societies and the county, President Petrie will hold a joint conference with all local presidents and vice-presidents in July 1970. Topics of mutual concern will be explored.

Dr. Petrie reported that the Hartford County Foundation project has reached the stage of surveying the membership as to their willingness to participate. He also reported that in New Hampshire, the MEDEX plan has reached a relatively advanced stage of implementation in some areas. Dr. Dorman, President of the AMA, with whom President Petrie chatted for about twenty minutes in New Hampshire, urged that organized medicine should increase communications with medical students. Dr. Dorman stressed the benefits of having S.A.M.A. chapters in all states.

Like his predecessor, Past President Kurt Pelz, President Petrie urged that the office of President be increased to a two year term so that programs once started can be followed through to logical and successful conclusions.

Dr. Louis Cappucci, Chairman of the Public Relations Committee, announced the birth of a new quarterly County publication to be called *Issues and Insight*, which made its debut in June. He also announced that a Speaker's Bureau is being formed. Further, for the Fall, the T.V. and radio media will be entered to project the New Haven County Medical Association's involvement with the community.

A county-wide Emergency and Disaster Committee has been formed in view of recent threats of civil disorder, and in view of the increasing role that accident rooms are playing in medical care delivery.

Dr. Bernard Burnham, Chairman of the Committee on State Legislation, pointed out that "price controls" have already been placed on the medical profession by the calling for a freeze at the 75th percentile of 1969 Medicare-Medicaid fees by HEW and the House Ways and Means Committee.

During and after the dinner meeting, seven Provisory members participated in the Indoctrination and Orientation program under the leadership of Credentials and Orientation Committee Chairman, Dr. John Hoffer. Following the program these seven Provisory members became Active members with full voting privilege. They are: Remo Fabbri, Jr., New Haven; Chester S. Kucinski, New Haven; David F. Musto, New Haven; Daniel Schubert, West Haven; Marc J. Taylor, West Haven; Joseph A. Vincitorio, Waterbury; Donald J. Weber, Waterbury.

Respectfully submitted,
William L. West, M.D., Clerk

Welcome, New Members

Middlesex County

Fahrettin Alptekin, M.D., Box 351, Middletown, Conn. 06457.

Patrick R. Concannon, M.D., 589 Old Saybrook Road, Middletown, Conn. 06457.

Allen B. Silberstein, M.D., 51 Prospect Street, Portland, Conn. 06480.

New London County

Edwin M. Clayton, M.D., Lawrence & Memorial Hospitals, New London, Conn. 06320.

Edward E. Edgar, M. D., Black Oak Drive, East Lyme, Conn. 06333.

James M. Hollister, M.D., 167 Broad Street, Groton, Conn. 06340.

Gilles A. Marchand, M.D., 425 Montauk Avenue, New London, Conn. 06320.

Arthur H. Mensch, M.D., Lawrence & Memorial Hospitals, New London, Conn. 06320.

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From the

Connecticut Regional Medical Program

(Introduction: The rapid development in recent years of Coronary Care Units in Connecticut hospitals demonstrates the serious concern about coronary disease and its high mortality. At present eight hospitals have specialized Coronary Care Units, ten have combined Intensive-Coronary Care Units, twelve have Intensive Care Units, and only five have no organized facilities. A recent State Health Department inventory of the coronary care capability within each general hospital, together with consultation with cardiologists throughout the state, suggested the need for a regional training program for community physicians through a brief but intensive clinical-educational experience demonstrating the latest advances in the care of patients with coronary artery disease. It was approved by the CRMP Advisory Board in 1968 and launched in May of the following year under the auspices of the Hospital of St. Raphael and the Yale University School of Medicine. Director of the program is Oscar Roth, M.D., New Haven cardiologist. It is also approved and supported by the Connecticut Heart Association and recognized for 50 hours of formal credit by the Connecticut Academy of General Practice. The program permits the community physician to leave his practice for a two-week period, with compensation for his time, and to become a resident of either hospital in order to acquire practical knowledge and experience in the aggressive care of myocardial infarction. Five courses have been given so far this year and the remaining seven courses are fully subscribed, indicating the need for continuing the program in 1971 if funds are available. Lavius A. Robinson Jr., M.D., General Practitioner of Danielson, one of 67 physicians who have completed this training, was asked by CRMP to describe the effect the program has had on his practice. His account follows.)

Like many other middle-aged active practitioners, I have had great difficulty in keeping up with the literature. The demands of family practice, community activities, church and family always seem to be usurping scheduled reading time. In addition, there are many things that have occurred since I was graduated from medical school that cannot be read in the journals—they must be demonstrated and appreciated by the senses. When I heard of Dr. Oscar Roth's Coronary Care Program at its inception, I was enthusiastic about it, and was fortunate enough to be enrolled in the first group.

It felt good to have the demands of practice removed, to be away from the stresses of the family and to study again full time. I enjoyed the stimulation of the house officers, and in particular, time to get into the Sterling Medical Library and really study in depth. The course has a nice balance in didactic material, dialogue, patient care as well as audio-visual aids.

The fourth heart sound was a complete new concept to me and its appreciation now in the handling of my patients has been of real value. This is one item that just could not be appreciated from reading the literature alone and the teaching aid using both the eye and the ear to appreciate the presence of this sound seems the easiest way to learn.

I can say that as a result of the course I feel more confident in the diagnosis of angina, coronary insufficiency and myocardial infarction. I can now diagnose most arrhythmias in the intensive care unit and treat them effectively and with assurance. Since the course, I have started anti-arrhythmic therapy of suspected coronairies on house calls or immediately in the emergency room—wherever they are seen first, using both intravenous Lidocaine and intramuscular Lidocaine to tide them over, especially on the ambulance ride from home to the hospital. I also now get coronary patients out of bed sooner and work harder at the relief of anxiety and apprehension earlier in the course of their disease before they are told their diagnosis. I have had four cases of ventricular fibrillation successfully converted, several problems of congestive heart failure associated with myocardial infarction and two cases of severe cardiogenic shock who have been discharged from the hospital alive. There is no question in my mind that the handling of these cases has been much more adept since attaining the knowledge that I gained from taking this course.

I would hope that this experience in post-graduate medical education will just be a beginning. I know in my own practice that I could use a two-week review in many major areas and that my patients would benefit directly by my increased knowledge. I am convinced that better health care could be delivered to all the residents of the State of Connecticut if all physicians voluntarily participated in this type of program.

I am of the personal opinion that the licensing of a physician for life without re-examination or at least, re-certification of satisfactory completion of courses of this nature, is a concept that needs a long, hard and fresh look.

Lavius A. Robinson, Jr., M.D.

News From Yale University School Of Medicine

Dean F. C. Redlich of the Yale School of Medicine outlined recently his views about the political activities of people in the medical and health fields, and about the academic options being planned at the School to allow time for these activities next fall.

"Our overriding principles must be that no learning or service experience should be lost, nor should any person not wishing to engage in political activities be coerced to do so," Dean Redlich said in a memo to faculty and students.

". . . there is no question but that the gradually emerging new contributions to medical leadership have had and will continue to have a salutary effect on both the political atmosphere and the political actions of this nation.

"We as a nation cannot afford the provocative gestures or the riotous emotions which have characterized political dissent in the past. We need, instead, a nation of thinking citizens who have invested their time and perhaps risked their position so that peace and justice can be the predominant themes of our times," he stated.

Referring to the appearance of medical students at the Connecticut State and New Haven County medical society meetings, Dean Redlich said that their reception "reflected great credit on all parties involved, hosts and guests, representatives and constituents."

Dean Redlich also noted that "all classes missed in May were subsequently made up" through the "hard work of students and faculty members and with the guidance of the academic options committee" of the medical school.

Dr. Collins

The first incumbent of the Harvey and Kate Cushing Professorship of Surgery at Yale is Dr. William Francis Collins, Jr.

A native of New Haven, Dr. Collins has been a Professor of Neurological Surgery at Yale since 1967 and is head of the Section of Neurosurgery in the Yale Department of Surgery. He was Professor and Chairman of the Division of Neurological Surgery at the Medical College of Virginia before coming to Yale.

Noted for his research in neurophysiology and neuroendocrinology, Dr. Collins has conducted studies of small nerve fiber systems in the spinal cord and brain which have been significant contributions to understanding the nervous system.

He is also well known as a clinician and teacher. The neurological surgery program under his direction at the Medical College of Virginia Hospital was considered one of the finest in the country.

He is the son of the late Dr. William F. Collins, a practitioner for many years in New Haven, and Mrs. Collins, now a resident of Florida. The senior Dr. Collins was also a Yale graduate, class of 1902, and took his degree in medicine at Yale in 1904.

The new Cushing professor was born in New Haven January 20, 1924. He graduated from Yale College in 1944 and from the Yale School of Medicine in 1947. He served his internship and residency at Barnes Hospital, St. Louis, Missouri, and was resident neurosurgeon there in 1952-1953. The following year he held a fellowship in neurophysiology at Washington University School of Medicine in St. Louis.

In 1954 Dr. Collins joined the faculty of Western Reserve University School of Medicine as an Instructor in Neurosurgery. He was promoted to Assistant Professor in 1957 and to Associate Professor in 1960. He was appointed to a Professorship at the Medical College of Virginia in 1963, and to a Professorship at the Yale School of Medicine in 1967.

Dr. Collins is married to the former Gwendolyn R. Davis of Thornton, Washington. They live in New Haven with their three children.

CONNECTICUT PHYSICIANS' ART EXHIBITION

The Connecticut Physicians Art Association exhibit was held recently in conjunction with the Annual Meeting of the Connecticut State Medical Society in Hartford at the Hartford Hilton Hotel.

The "Best in Show" award was given to Diane Marinaro, wife of Dr. Nicholas Marinaro, Newington, for her oil painting "Spirits" and the John M. Freiheit award given by the New Haven County Medical Association was awarded to Dr. William Schneider of Rockville.

In the professional class in oil, Dr. Schneider received the 1st award for his painting "Interior" and Mrs. Ruth Waskowitz, wife of Dr. W. J. Waskowitz, New Britain, 2nd, "Simsbury Countryside". Professional water color: 1st award, Dr. Tibor de Cholnoky, Greenwich, "Straw Flowers"; 2nd, Mrs. Ralph Gilman, Storrs, "Dionis from the Sea" and Honorable Mention to Mrs. Wei Chin Chang, Windsor, "Stream Fishing". Mixed Media: 1st was awarded to Dr. Sophie Trent, Meriden for her Tissue Collage "Vermont Autumn". Sculpture, Intermediate: 1st award, Mrs. Frances Kim of New Haven, "David's Paper Mill"; also 2nd to Mrs. Kim for her metal sculpture "Twenty Fathoms" and Honorable Mention to Mrs. Hazel Rentsch of Derby "Mother Earth". Sculpture beginner: 1st award, Dr. Peter Gram of Manchester "Morning Gossip". Intermediate Oil: 1st award, was given to Carol Sirot, wife of Dr. Gustave Sirot, of New Haven for her painting "Ocean"; 2nd to Dr. Edward Williams, Naugatuck, "Organ Grinder" and also Honorable Mention to Dr. Williams for his portrait "Hod Carrier". In water color: the 1st award was given to Dr. Stuart Danoff, Stamford, for his sea gull water color "Harbor Scene"; 2nd to Carol Sirot, New Haven, "Methodist Campground Home", and Honorable Mention to Mrs. Lowell Olson, North Haven, "Nude". In Black and White drawings, the first award went to Dr. Robert Lowman of New Haven for his pen and ink sketch, 2nd to Mrs. John Murphy of West Hartford for her pencil drawing "Study #1" and Honorable Mention to Dr. Edward Nichols, Ink drawing "Figures".

In the children's class the 1st was given to Eileen Shapiro, daughter of Dr. B. S. Shapiro, Orange, for her collage "A Doctor's World" and 2nd to James C. Coyle, son of Dr. William Coyle, Derby for his poster color, untitled.

Photography: 1st award, Jeffry Oster, Son of Dr. Kurt Oster, Bridgeport, "The Old Creek", 2nd, Dr. John A. Woodworth, Moosup, "Minemsha Dream" and Honorable Mention to Dr. Kurt Oster, "Smugglers Haven".

The Chairman of the 1970 exhibition was Dr. Eugene Rightmeyer, President of the Connecticut Physicians' Art Association, assisted by Mrs. Orvan Hess of North Haven, Vice President, and Mrs. John Murphy of West Hartford, Art Chairman Woman's Auxiliary of the Connecticut State Medical Society.

Judges For The Connecticut Physicians' Art Association

The judges for the Art Exhibit were: Mrs. Ethel Stauffer of Hamden, painter and teacher, past president of the New Haven Paint and Clay Club, member of the Connecticut Academy of Fine Arts and the Pennsylvania Academy of Fine Arts; Gail W. Martin of Hartford, Professor of Art at the University of Hartford, member of the Connecticut Water Color Society and the Connecticut Academy of Fine Arts; and Mitchell Pappas of Hartford, painter and Associate Professor of Fine Arts at Trinity College, Director of the Austin Art Center, member of the Connecticut Water Color Society and the Connecticut Academy of Fine Arts.

Science News

Traffic Pollution And Mental Efficiency

(*Nature*. 225: 95, January 3, 1970, Lewis J., et al.) These authors compared the performance in a number of mental tests of subjects age 18-28 breathing pure air with their performance when breathing air pumped in from a moderately busy road (average traffic flow 830 passenger carrying units). They tested auditory, vigilance, addition, sentence comprehension and digit copying.

Mean digit height in the digit copying test did not differ between the two conditions. This indicates that the skill in actually handling the car is much less susceptible to fatigue and stress. There is, however, a marked decrease in the mental efficiency of subjects breathing air taken from the road.

The results suggest that traffic pollution may play an important and hitherto unsuspected part in precipitating road accidents.—L.H.N.

Viruses And Cancer

(*Nature* 225: 226, January 17, 1970 Aaronson, Hartley and Tadaro) Isolated stable cell lines from embryos of inbred BALB/e mice which became tumorigenic when maintained in tissue culture on a schedule of rapid subculturing at high cell densities.

Several of these cell lines also began to produce murine leukemia virus after many passages in culture, even though there was no evidence of the virus in the original embryo culture from which the cell lines were selected or in the cell lines themselves at the early stages of the experiment.

Three possible explanations were considered (a) accidental infections (b) cells were all the time infected with the virus but with amounts too small to be detected. (c) mouse cells may have in a repressed form the information needed to make murine leukemia virus. Aaronson et al after careful thought decided the last explanation to be the most probable.

The idea that the mouse cells contain information for leukemia virus production is a very novel one but extremely difficult to prove. However, it is consistent with the hypothesis that cancer results from the induction of latent RNA viruses.—L.H.N.

The Association Between Salivary Gland Cancer And Breast Cancer

(Moertel, Charles G. and Elveback, Lila R.: *JAMA*, 210: 306, October 13, 1969) The tendency for multiple primary cancers to develop in the same or contiguous epithelial surfaces or in bilaterally paired organs has been thoroughly documented for many years. Although a few claims have been made, there has been no convincing evidence of a predisposition for multiple cancers to develop in different organs or tissues.

In 1968, however, Berg and associates, after a review of case material at the New York Memorial and James Ewing hospitals, reported an excess of total cancers in patients with previous salivary gland cancer, and a unique association between salivary gland and breast cancer. Seven instances of breast carcinoma were noted for 880 patient-years of follow-up information on women with previous salivary gland carcinoma, and the authors stated "the probability of a chance of clustering of breast cancers among patients with salivary gland cancer who really have no excess risk is extremely low, about 0.004%." The fact that such an association had never been previously noted in the literature was interpreted as an indication that other reviewers were likely to have had enough patients to make the association clear. In conclusion, the physician was cautioned to special vigilance in examining the breasts in routine follow-up of women with salivary gland cancer.

The present study was undertaken by the method of Berg and associates to determine whether such an association could be validated.—L.H.N.

Effects Of Burns On The Heart

(*JAMA*, 211, 2130, March 30, 1970, Joshi, Vijay V.) Seven fatal cases of burned children showed that congestive heart-failure was a major factor in their deaths.

The patients had infected burns, prolonged clinical course, anemia, episodes of hypokalemia and hyperkalemia, systemic hypertension and hypoproteinemia. At autopsy, all cases showed cardiomegaly with focal inflammatory and degenerative lesions of the myocardium. This report is to alert physicians to the possibility of congestive heart-failure in burned children.—L.H.N.

Acid Reports On Acid

(*Nature,* 225: 4, April 4, 1970) LSD can awake the urge to kill oneself or others. It may cause deep depression or violent swings of mood, particularly in people who are unstable and contrary to popular belief, taking LSD may be dangerous even for those who are emotionaly mature. It is in a class with heroin considered to be the most dangerous.

Claims that LSD can help people to solve their personal and intellectual problems are generally not confirmed by psychological measurements. There is also no conclusive evidence that LSD is better than any other kind of treatment in treating patients such as chronic alcoholics or those with psychosexual difficulties although there is nothing to suppose that in responsible hands, LSD is exceptionally dangerous.

Suggestions that the drug may cause chromosomal damage to the sex cells have not been confirmed.—L.H.N.

Marihuana Use Among Urban Adults

(*Science,* 166: 1544, Dec. 19, 1969, Manheimer, Dean I., Mellinger, Glen D., Balter, Mitchell B.) The primary finding that emerges from this study is that a relatively high proportion of young people 18-34 in San Francisco, have used Marihuana one or more times. The proportion in this age group who have used this drug is as great among nonstudents as among students.

The data generally confirm the view that marijuna use tends to be associated with an "antiestablishment" point of view and to some extent with a search for a new ethic.

Nevertheless, the majority of men and women who have used the drug appear to be reasonably conventional.—L.H.N.

Sleep Patterns In Natural And Mandrax And Tuinal Induced Sleep

(*Canad. Med. Assoc. Jr.,* 102, 506, March 1970, Davision, K., Duffy, J. P., Osselton, J. W.) A within subject comparison of the effects on the overnight sleep ECG of 1 tablet of Mandrax (containing methaqualone) base 250 mg and diphenyl-hydramine hydrochloride 25 mg) and 200 mg Tuinal (equal parts of quinol barbitone sodium and amylobarbitone) in 14 normal subjects is reported.

Mandrax induced sleep was not significantly different from natural sleep in duration of light, moderate, deep and REM phases.

Tuinal produced a significant reduction in REM sleep compared with natural sleep and with Mandrax-induced sleep.—L.H.N.

Members of the Connecticut State Medical Society reading papers before other organizations are requested to submit their papers to the JOURNAL for consideration by the Board of Editors for publication. Please send them to:

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Hair May Be Used To Gauge Protein Deficit

(*JAMA,* 211: 1469, March 2, 1970) A lock of hair can be a key to hidden hunger, reported R. G. Crounse, Professor of Dermatology at the Medical College of Georgia.

Protein malnutrition shows itself being very late in serum protein changes. The hair root volume and protein amount can be readily measured and show protein changes early and can be measured precisely.

He found protein deficiency in hair of malnourished mental cases and from children in Biafra.

The method requires fifteen to 60 hairs plucked from the occipital scalp. In severe malnutrition values as low as 2 ug/hair were found. In well fed individuals the hair contained 10 ug to 30 ug of alkali-soluble protein per intact, growing hair root.—L.H.N.

The Genetics Of Schizophrenia And Schizoid

(*Science.* 167: 249, January 16, 1970, Heston, L. L.) Genic factors in the development of schizophrenia have now been definitely established. However, it is clear that environment too plays a role. Schizoids are relatives of schizophrenics who also have psychiatric disorders.

It is estimated that 4 percent at least of the general population will be afflicted with schizoid-schizophrenic disease. Among monozygotic twins one may be schizoid and the other schizophrenic.

The proportion of affected first-degree relatives and the segregation of affected individuals within families closely approximates theoretical expectations based on the hypothesis of a defect in a single autosomal dominant gene. However, modifying traits play a significant role.

Emphasis by the author is placed on hypotheses which can be tested by future research.—L.H.N.

Herpes Zoster After Exposure To Chickenpox

(*JAMA,* 211, 1831, March 16, 1970, Berlin, B. S., Campbell, Thomas.) Chickenpox developed in an intern attending a retired nurse 16 days after his initial contact with her. One day before the onset of his rash, the intern had close contact with a patient who had been receiving immunosuppressive therapy for a kidney transplant.

After an appropriate incubation period typical herpes zoster developed in this patient. The chain of infection involving these temporally related cases presents strong justification for considering some cases of zoster to be exogenous infections.—L.H.N.

Marijuana

Whatever its effects on users, marijuana is producing much anxiety among parents, and many physicians are concerned or uncertain about their responses when the anxiety brings parents to the consulting room. What advice can the physician honestly give about the hazards of smoking marijuana?

In trying to provide an answer to this question, The Medical Letter consulted many psychiatrists, pharmacologists, and others who have investigated or otherwise been professionally concerned with the problem. There was sharp disagreement among them, with no consensus that would permit a confident answer. As one consultant pointed out, extreme caution is necessary in making any judgments because of the lack of reliable information. The best The Medical Letter can do at this point is to provide background information that may be useful.

There is great variability in the effects of smoking marijuana resulting from variations in the plant, Cannabis sativa or Indian hemp, from which it is prepared, the way it is smoked, the social setting, and the experience and expectations of the user. The pharmacologic activity of the plant results mainly from the tetrahydrocannabinol (THC) content of its flowering tops and upper leaves, and the THC content may vary from near zero to two per cent or more depending upon the variety, the soil, the heat, humidity and other climatic conditions, whether the plant is wild or cultivated, and the time of harvesting. Prolonged storage reduces activity. The stems and seeds are virtually inactive. Marijuana prepared from the entire plant is likely to have relatively little activity; if only the upper leaves and flowering tops are used, activity is likely to be much greater. THC has been synthesized, but material sold as synthetic TMC on the street is likely to be found on analysis to contain no THC; it may contain phencyclidine (a veterinary anesthetic), mescaline, methamphetamine, LSD, or other drugs.

Hashish, the brown resin collected from the tops and leaves of high quality marijuana, is far more potent than the plant parts. There has been little experience with hashish in the United States thus far, but its use appears to be increasing. Since it has a much higher content of THC, its adverse effects are likely to be more severe than those seen with marijuana.

Mode Of Use

When marijuana is smoked, maximum effect is obtained with deep inhalation and retention of the smoke as long as possible. A single deep inhalation of a high quality cigarette may have a greater effect than smoke from several cigarettes of low grade material. The onset of action of a potent preparation is within minutes; the effects may continue for at least an hour or two, and can be maintained by intermittent inhalation of additional material. Marijuana can be taken orally; as with other oral drugs, the onset of action is delayed, but the effects may last for many hours.

Psychologic Effects

Time perception may be altered. Dysphoria occurs occasionally, though a feeling of relaxation or euphoria is more common. Anxiety and occasional feelings of suspiciousness may be present. A novice may show fearfulness and confusion about the feelings he is experiencing. Delusions are likely to occur only with high doses. Although hashish (if it is not heavily adulterated) may cause hallucinations, marijuana rarely does, except with very high doses. Like users of alcohol and other disinhibiting agents, the marijuana user may behave in an unrestrained manner. Marijuana, like alcohol, has no true aphrodisiac properties. Thought may be dreamlike and fantasy-laden, but the person can usually "pull himself together" when necessary and perform adequately. Acute adverse mental reactions have been reported from Vietnam and India, where the marijuana has a high THC content. Whether the reactions are due to the THC or to an adulterant is not certain, however.

The habitual user of marijuana sometimes becomes passive and withdrawn. The long-term effects are yet to be determined, but there is a growing body of evidence that the continuing heavy user, or "pothead," becomes so involved in the process of securing and using the drug that his drive and motivation for other activities are impaired. In countries where strong preparations of cannabis have been available for centuries, an extensive literature describing apathy, loss of drive, psychoses, and dementia with heavy or habitual use exists, but this literature is mainly anecdotal, and cause-and-effect relationships are not clear. A carefully controlled study of populations where cannabis use is traditional would assist in the scientific evaluation of the drug.

The question concerning the escalation to heroin by the marijuana user cannot be answered simply. Many heroin addicts report that they began their illicit drug careers with marijuana, and the drug subculture centered mainly on marijuana doubtless increases the exposure of susceptible persons to addicting drugs. Nevertheless, the great majority of marijuana smokers never go on to the opiates.

Physical Effects

The most frequent physical effect of marijuana is conjunctival injection (red eye). This is not due to the smoke, for it also occurs when preparations containing THC are swallowed. Slight unsteadiness, tremulousness, and impairment of coordination may occur. Some persons experience drowsiness or feelings of hunger. Speech may be slowed and halting. Recall for the immediate past may at times be defective. Although one Medical Letter consultant has found evidence to the contrary, smokers are not generally thought to acquire tolerance of marijuana. An abstinence syndrome in habitual smokers of large amounts of hashish has been described; it may merely reflect the psychological reaction of a dependent person.

Relatively little work on the cytogenetic effects of cannabis has been done, but so far results have been negative. Obviously, all cannabis preparations should be avoided during pregnancy and lactation. As with tobacco, smoking marijuana over many years may cause bronchitis and emphysema; the possibility of carcinoma of the lungs with long continued heavy use cannot be discounted.

Treatment

The treatment of acute cannabis reactions consists largely of reassurance and support. A sedative may be necessary. The infrequent psychotic reactions with marijuana ordinarily subside in a few days.

Conclusion

Far too little is known about the physical and mental effects of marijuana, and studies that will provide reliable data are badly needed. In the absence of such studies, it can only be said that most persons who use marijuasa in moderation for a time are unlikely to suffer any lasting harmful effects. There may be immediate undesirable effects on behavior and achievement depending on the potency of the mixture used, the frequency and manner of use, and the personality of the user. The effects of long-term use are not known.

There is no direct association between the smoking of marijuana and the use of heroin, and most users of marijuana do not go on to heroin. Nevertheless, marijuana smoking helps generate drug-oriented groups in which the interest of a single member in other drugs, such as hashish or heroin, can quickly infect the group. Unfortunately, hashish is becoming increasingly available, though there is some question about the potency of much of what is sold as hashish in the United States. Adulterants sometimes used with hashish may present hazards. Whatever the clinical problems in the use of marijuana, almost every Medical Letter consultant opposed the harsh legal penalties for its possession for personal use.

Reprinted from the Medical Letter on Drugs and Therapeutics, New York, N.Y. Vol. 12, No. 8, April 17, 1970.

Possible Basis For The Cariostatic Effect Of Inorganic Phosphates

(*Nature* 2251, 1249, March 28, 1970, Pruitt, K. M., Jamieson, A. D., Caldwell, R. C.) Inorganic phosphates are effective in reducing dental caries when added as supplements to cariogenic diets fed to rodents and when added to chewing gums and to breakfast cereal eaten by children.

The authors studied whether this effect was caused by differential election of protein absorbed on enamel or whether it modified the enamel surface in such a way as to alter the acquired surface layer of the tooth.

These experiments are recounted in detail and suggest the hypothesis that the basis of the cariostatic effect of inorganic phosphate is a modification of the composition of the protein layer absorbed on enamel. In the case of sodium trimetaphosphate, an alteration results in a change in the affinity of various salivary protein for the enamel surface.—L.H.N.

Chromosome Abnormalities In Patients Treated With Chlorpromazine Perphenazine And Lysergide

(*British Med. Jr.*, 3, 634, 1969, Nielsen, J., Frederich, V. and Tsuboi, T.) In a chromosome study on leukocyte cultures made from 13 patients treated with chlorpromazine, 15 treated with perphenazine and 9 treated with lysergide, there was a significantly higher frequency of gap breaks and hypodiploid cells in the patients treated with perphenazine and lysergide than in the 41 control studied.

It is concluded that if some drugs can induce major chromosome abnormalities and less toxic alternatives are available the latter should be used in preference.—L.H.N.

Knock At Lead

(*Nature*, 225, 1181, March 28, 1970) Lead free gasoline is replacing leaded types because lead shortens the life of catalysts used to treat automobile exhaust fumes. The catalysts treaters oxidize such compounds as waste hydrocarbons, carbon monoxide oxides of nitrogen which are more serious pollutants at least in the first degree than is tetraethyl lead that is added to gasoline to inhibit knocking.

Some say that at present levels the use of lead in gasoline is no danger to health. Others, however, claim that the "safety margin between the present lead asborption for a person living in the city and that absorption which gives rise to chronic damage in man is apparently very small, possibly completely non-existent".

The amount of lead in the atmosphere typically about 3 micrograms per cubic meters for Stockholm, is keeping step with the increase in the number of motor cars on the Hollywood freeway on a Saturday. Danielson cites a single measurement of 71.3 micrograms per cubic meter. About 25 micrograms per cubic meter seems a typical value for rushhours in Los Angeles. Danielson claims half of this is absorbed by man. Absorption of lead from food is already close to his estimate of the maximum permissible daily dose of about 5-10 micrograms of lead, which means that there is a good case for reducing the contribution of lead from gasoline to nil.

The absorption of lead from inhaled air is estimated by Danielson as about 22 micrograms per day for a person breathing a concentration of 3 micrograms per cubic meter.—L.H.N.

Choroid Plexus And Cerebrospinal Fluid Production

(*Science*, 166, 1514, Dec. 19, 1969. Milhorat, Thomas H.) Acute progressive hydrocephalus occurred in 76 rhesus monkeys undergoing ventricular obstruction 2-6 months after choroid plexectomy and was only slightly less pronounced than in 73 non pleexectomized animals with similar ventricular obstructions.

The composition of cerebrospinal fluid after choroid plexectomy was essentially normal. Experiments with ventricular perfusion technics indicate only a slight reduction in cerebrospinal fluid production after choroid plexectomy.

Thus the choroid plexus is probably not the sole or even the major source of cerebrospinal fluid within the ventricular system.—L.H.N.

Beware Of The Drinking Water

(*Nature,* 225, 1180, March 28, 1970. Britain's water supply could become contaminated with unusual toxic chemicals which would not show up in routine tests conducted by water authorities—a report published by the Institute of Wales Engineers. The report also proposes sweeping changes in the organization of water resources.

The institution points out that chemicals of unknown toxicity are being poured into rivers and many end up in the water supply. There is also the possibility that illicit dumping and unexpected events such as the accidental leakage of chemicals and oils from road tankers could result in serious contamination.

During the last 5 years, 312 cases of surface water being polluted have been reported by 140 authorities. The institution estimates that about 25 per cent of Britain's water supplies are drawn from polluted waters and another 25 per cent come from rivers which are liable to sudden unexpected pollution. "Safety" margins are becoming too narrow in relation to the increased use of frequently or heavily polluted waters for public supply sources.

There is a need for more scientists using modern laboratory equipment to monitor the risks.—L.H.N.

L-Dopa: Effect On Concentrations Of Dopamine, Norepinephrine, And Serotonin In Brains Of Mice

(*Science,* 168, 849, May 15, 1970, Everett, G. M., Borcherding, J. W.) Large doses of l-dopa given to mice produced marked increases in brain dopamine, no change in norepinephrine, and a remarkable decrease in brain serotonin.

This reduction apparently results from a release or displacement, or both of serotonin from its storage sites.

The possibility of a similar decrease of brain serotonin occurring in patients treated with l-dopa must be considered highly likely and may be pertinent to the observed therapeutic effects, the side effects or both.—L.H.N.

Anesthesia After Myocardial Infarction

(*Minn. Med.* 52, 1733, 1969, Tarhan S., Moffitt, E. A.) The mortality rate of patients with recent myocardial infarction is high if they are subjected to anesthesia and operation.

Elective operations should be delayed until after a healing period of 3 months. Prior to operation such patients should be brought to the best possible state of compensation.

During operation the patient should have a light level of anesthesia, adequately controlled ventilation and oxygenation and abolition of undesirable vagal reflexes. Hemodynamics must be carefully observed and corrected or supported as needed.

Postoperative myocardial infarction is frequent and associated with a high mortality rate. Such patients should be kept under constant surveilance after the operation.

Hypoxemia commonly occurs after anesthesia requiring treatment with oxygen and vigorous efforts to reduce atelectasis.—L.H.N.

Dyspnea And Angina

(*Med. J. Aust.*: 1, 1066, 1969, Gault, J. E.) Of a series of 78 patients with angina pectoris, half reported having also dyspnea with the anginal attack. Hyperventilation accounted for some and left ventricular failure for others.

The occurrence of shortness of breath in association with anginal pain is probably from transient left ventricular failure associated with the attack. The failure subsides with the cessation of effort and is unresponsive to digitalis and diuretics. It should be regarded as a part of the anginal symptom complex.—L.H.N.

Social Effects Of Myocardial Infarction In Men Under Age 50: Review After One To Eight Years

(*Med J. Aust.* 2, 125, 1969, Brown, L. B., Antic R., Hetzel, B. S.) Wide individual differences were observed in the technics of adjustment by the patient following an infarct. In assessing the "quality of life", 18 out of 24 patients reported some deterioration. This includes half of the moderate infarct group. Six, however, seemed to derive more satisfaction.

Reasons for the deterioration ranged from work problems to a wife's desertion. No single factor explains the maintenance or disruption of the patients lives and only a few were anxious, aggressive overreactors.

The main conclusions relate to a discrepancy between medical assessments and patients estimates of their functional state and absence of any common pattern of personality or social background.

Environmental support through work and social involvement seems to have been critical in contributing to the maintenance of a satisfying "quality of life" and consequent recovery from illness.

Too often the ordinary social environment was not activated to provide needed support and a smooth rehabilitation for the patient following his discharge from the hospital.—L.H.N.

Fine-Particle Humidifiers: Source Of Pseudomonas Aeruginosa Infections In A Respiratory-Disease Unit

(*New Engl. Jr. Medicine,* 282, 531, March 5, 1970, Grieble, Hans G., et al) In a pulmonary-disease ward containing a respiratory-disease intensive-care unit, 9 per cent of the patients in the ward and one fifth to one third of those in the intensive-care unit harbored Pseudomonas aeruginosa in their respiratory tracts. Eight patients acquired pseudomonas pumonary infections in the hospital.

The fine-particle aerosal from unheated humidifiers was shown to cause heavy environmental contamination by Ps.aeruginosa. Each of the four respirators in the intensive-care unit propagated 6 x 10^6 organisms per day. Decontamination of humidifiers by various means was unsatisfactory, and their use had to be discontinued.—L.H.N.

Use Of Digitalis In Acute Myocardial Infarction

(*The Heart Bulletin:* 18, 106 1969, Marcus, F. I.) Digitalis is indicated for patients with atrial flutter, fibrillation and tachycardia with rapid ventricular rate. If the arrhythmia is accompanied by hypotension or heart failure, the physician may elect cardioversion.

Digitalis may be added to antiarrhythmic agents when the patient is suffering from recurrent ventricular arrhythmias in order to improve contractility and functional efficiency.

Digitalis is not indicated in AV block unless there is inserted a cardiac pace-maker.

Digitalis can be useful in congestive heart failure complicating acute myocardial infarction. But some patients show little or no response. For this reason, diuretics are used in conjunction with digitalis.

Isoproterenol is more effective than digitalis in patients with shock.

There is no evidence to support the use of digitalis prophylactically or in patients with early signs of left ventricular failure.

Avoid rapid I.V. injections of digitalis. It may weaken the heart and induce ventricular fibrillation.—L.H.N.

The Natural History And Management Of Radiation Induced Injury Of The Gastro-intestinal Tract

(*Ann. Surg.,* 170, 369, 1969, DeGrosse, J. J., et al.) 100 patients were hospitalized because of radiation induced injury of the gastro-intestinal tract. They were mostly related to rectum and colon, one had carcinoma of the rectum.

Death was attributed to recurrent cancer in 28 and radiation injury in 22.

There was a significant correlation between gastro-intestinal radiation injury and hypertension and less so diabetes, artero-sclerosis. In 25 patients injury only became manifest 2 years later. There was a relationship between low splanchnic blood flow from systemic vascular disease and radiation vasculitis especially at points of fixation of the intestine. Operation of relatively minor complaints should be avoided.—L.H.N.

Dynamic Clinical Studies With Radioisotopes And Scintillation Camera. IV. ^{99m} Tc-Sodium Pertechnetate Cardiac Blood Flow Studies

(*J. Nuclear Medicine:* 10, 270, 1969, Burke, G., Halko, A., Goldberg, D.) Right heart to left heart transit time can be studied by injecting a bolus in the antecubital vein with the subject supine.

Visualization of the cardiac chambers and cardiopulmonary blood flow achieved with the scintillation camera compares favorably with that obtained in conventional angiocardiography. The technique has been found valuable in determining relative cardiac chamber size, detection of intracardiac shunts and demonstration of pericardial effusions.

The method is without hazard to the patient and appears to be of significant diagnostic value in a variety of cardiac disorders.—L.H.N.

Evaluation Of A Program For Preventing Adolescent Pregnancy

(*New Engl. Jr. Med.:* 282, 1078, 1970, Cordes, Leon, et al.) Birth-control services with intensive individual and group counseling were provided for preventing pregnancy in sexually active multiparous adolescents. During the first 2 years, 100 girls were placed on contraception.

Despite intensive followup efforts, only 50 per cent remained active with the program one year after admission. Almost half the younger adolescents were still active in the program at the end of 2 years. The only side effect was weight gain, especially by the girls who were already overweight at the time of admission to the program.

These observations indicate the complexities involved and demonstrate the need for an interdisciplinary team approach in the prevention of adolescent pregnancy.—L.H.N.

Elevation Of Aortic Proline Hydroxylase: A Biochemical Defect In Experimental Arteriosclerosis

(*Science,* 168, 987, May 22, 1970, Fuller, G. C., Langner, R. O.) The authors studied relation of collagen synthesis in experimentally induced arteriosclerosis by measuring proline hydroxylase activity.

They produced gross aortic plaques in rabbits by daily injection of epinephrine and thyroxine for 4, 9, or 14 days.

Proline hydroxylase activity increased significantly after 4 days of treatment and reached a peak, 5-6 fold increase after 14 days of treatment.

The increase in enzyme activity correlated with the severity of observed arteriosclerosis and may be a possible biochemical defect in the aortas of rabbits with arteriosclerosis induced by injury.—L.H.N.

Soviet DDT Production

(*Science,* 168, 951, May 22, 1970) The Soviet Ministry of Agriculture has banned further production of the pesticide DDT "for the protection of food and fodder crops". The order, disclosed in a letter to Pravada, apparently does not affect the use of DDT already in stock.

The ministry also said it was taking steps to restrict the use of other pesticides, including zinc phosphides, which were recently blamed for the killing of rare wildlife.—L.H.N.

Thermal Pollution

(*Science,* 168, 951, May 22, 1970) The Federal Water Quality Administration has announced a strict thermal pollution policy for Lake Michigan forbidding the discharge of any fluid that would raise temperatures at the point of discharge by more than 1° Fahrenheit. The current standard, 3° Fahrenheit, applies to all states, but the new standard would apply only to Lake Michigan.

According to an agency spokesman, if the Great Lakes states do not adopt the new standard voluntarily, the agency can impose it after several months of hearings and legal maneuvers. The eventual cost to industrial users of the lake could run to millions.—L.H.N.

Marihuana Report

(*Science.* 168, 804, May 15, 1970) The House Select Committee on Crime has published a report on the hazards and effects of the use of marihuana. The findings of the report are:

1. Marihuana can cause psychological dependence.
2. Use of marihuana can introduce persons to a drug culture, which in turn may lead to experimentation with other drugs.
3. The effect of marihuana depends in large part on the mental set and milieu of its users.
4. 8-12 million persons in the United States have tried it at least once.
5. Courts customarily exercise leniency, especially with first offenders.

The Select Committee has asked the Surgeon General to prepare a report on marihuana similar to the one issued on the hazards and medical effects of smoking cigarettes.—L.H.N.

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Index to Advertisers

Arch Laboratories	479
Biochemical Procedures	475
Burroughs-Wellcome	bet 516 & 517
Campbell Soup Co.	bet 500 & 501
Classified Advertising	526
Conal Pharmaceutical, Inc.	bet 500 & 501
Connecticut Bank & Trust Co.	477
Dentocain Company	470
Dow Chemical Co.	bet 516 & 517
Arthur W. Eade	9
Geigy Pharmaceuticals	bet 516 & 517, 517
Geriatric Pharmaceutical Corp	6, 471
Hynson, Westcott & Dunning, Inc.	3
Lederle Laboratories	2, 5, 473
Eli Lilly & Co.	FC & 10
McNeil Laboratories	467
National Drug Co.	bet 468 & 469, bet 532 & 533
Poythress, Wm. P. and Co.	bet 516 & 517
Roche Laboratories	BC
Sanibel Hospital, Inc.	8
Schering Corporation	bet 484 & 485
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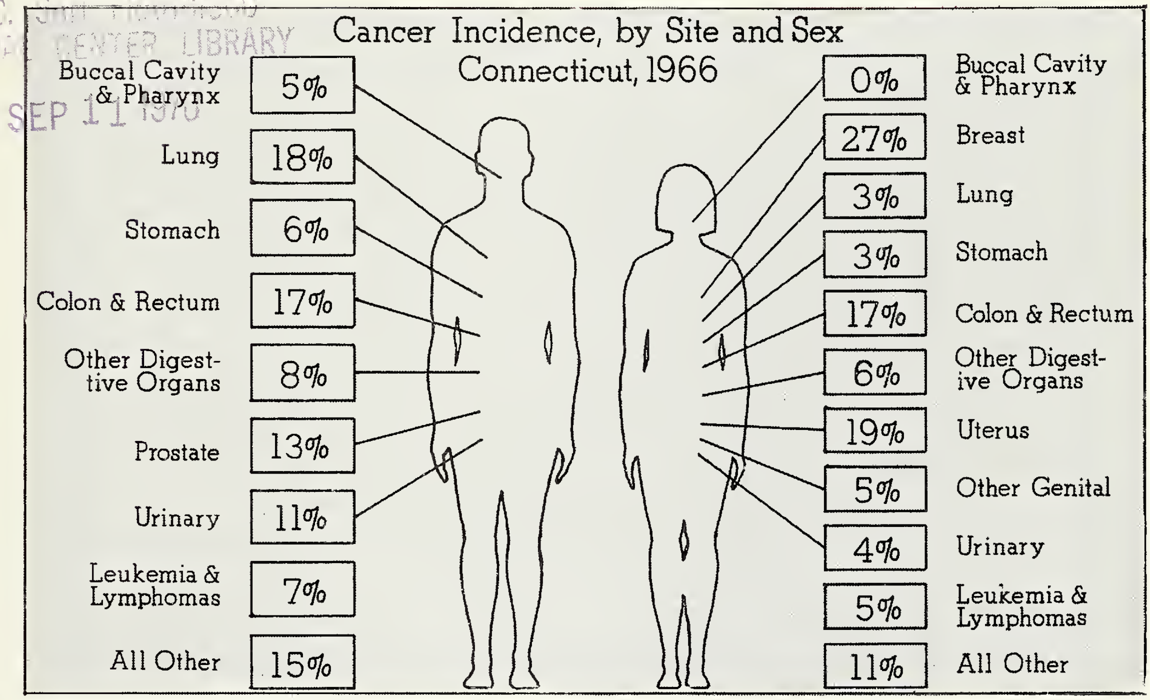

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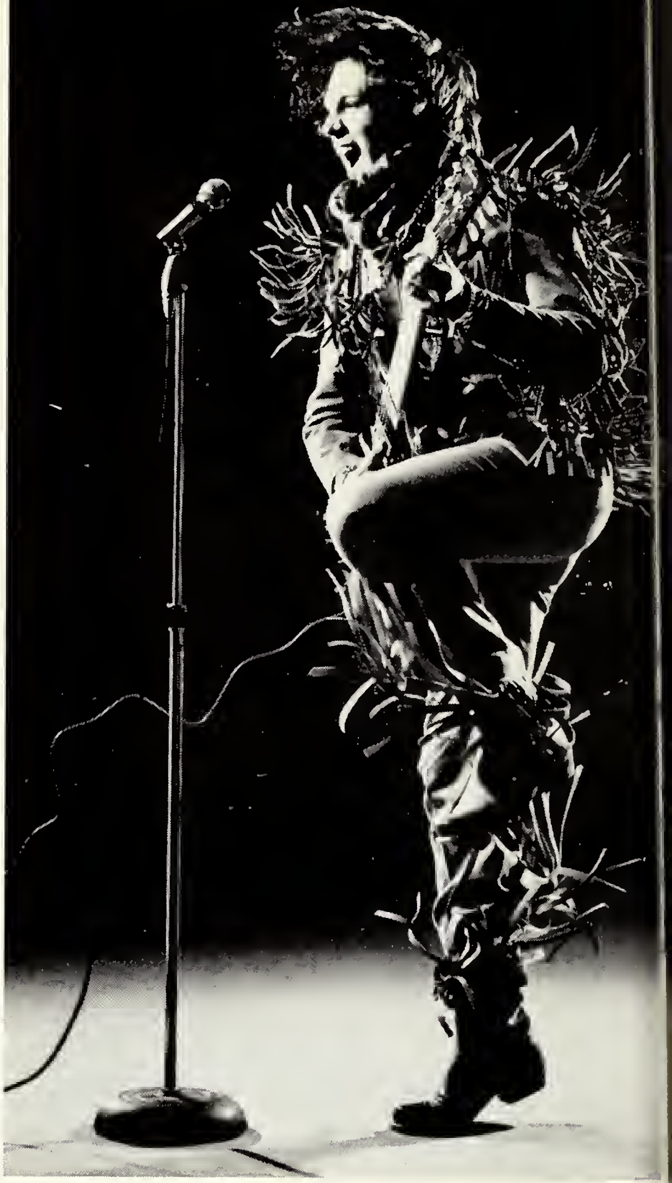

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CONTENTS

editorials

Controlling Human Fertility 541
Retirement Can Be A Waste of Manpower 542
To Treat Or Not To Treat The Mild Hypertensive 542
The Heroin Plague 544
Adaptations In Astronauts To Interplanetary Space Flights . 546
The Role Of Sympathetic Blockade In The Treatment Of Hyperthyroidism 547
Recent Progress In Anesthesiology 549
Cross Reactions Of Oncogenic Viruses 550
A British Clinician Speaks 553
Carbon Monoxide And Atherosclerosis 554

scientific

Hereditary Pancellular Lysosomal Gigantism (Chediak-Higashi Syndrome), *Frederick J. Flynn, Jr., M.D., Mary S. Coley, M.D., Ronald S. Beckett, M.D.,* and *B. Shannon Danes, M.D.* 557
Cancer Incidence, Mortality And Survival In Connecticut During The 1960's, *Barbara Christine, M.D., M.P.H., Paul D. Sullivan, B.A., Roger R. Connelly, M.Sc.* and *Franklin M. Foote, M.D., Dr., P.H.* 564
The Fractured Jaw, *Morton H. Goldberg, D.M.D., M.D., Albert Nemarich, D.D.S.* and *Robert Aslanian, D.D.S.* . . 570
Transposition Of The Great Arteries, *C. E. Anagnostopoulos, M.D., N. DeLeuchtenberg, M.D., N. S. Talner, M.D.* and *H. C. Stansel, Jr., M.D.* 573

departments

The President's Page 578
Physician's Placement Service 588
Woman's Auxiliary 592

miscellaneous

Anesthesiology Grand Rounds, *Samuel M. Lerner, M.D., John A. Kirchner, M.D.,* and *Frederick W. Hehre, M.D.* . . . 580
Law-Medicine Notes, *J. Alfred Fabro, M.D.* 583
Electrocardiogram Of The Month, *Hyman M. Chernoff, M.D.* 584
Letter-To-The-Editor 586
Connecticut Regional Medical Program 587
In Memoriam 590
Around The State 591
Space Diets In Medicine 595
Meetings 596
Science News 597
New Books In Review 599

Connecticut Medicine

editorials

Controlling Human Fertility

In a recent number of the *British Medical Bulletin* (*26*, 1, 1970) leading British Scientists discuss the problem of controlling human fertility. In the first three contributions we found an informative discussion of our present knowledge of the physiology of reproduction. Later papers consider the relief of infertility with gonadotropin or clomiphene. There are also papers on aspects of contraception and possible control of fertility in the male.

Crooke found that only 15 per cent of those attending a fertility clinic to be suffering from failure of ovulation. In such women, the prognosis has been revolutionized by the discovery of clomiphene citrate and the use of human gonadotropic hormones in selecting patients for treatment. The crucial investigation is the assay of urinary gonadotropins. If the level is high then the patient has no primordial follicles left in her ovaries which can respond to treatment with gonadotropins.

It is the patient with low or fluctuating levels in whom a response can be expected. There is, of course, a problem in monitoring dosage as evidenced by the number of multiple births reported after this form of therapy. At present human pituitary gonadotropins (HPG) or gonadotropins from human menopausal urine (HMG) are used. These contain a mixture of follicle stimulating and luteinizing hormone sequentially with human chorionic gonadotropin (HCG) containing luteinizing hormone. The side effects include rare local effects of injection, multiple births and the hyperstimulation syndrome in which the ovaries enlarge and become cystic and tender.

The alternative to these naturally occurring and exceedingly expensive gonadotropins is clomiphene. This substance though easier to administer than the gonadotropins is also less effective. Its response is easier to control, however, and multiple births are rare. Its site of action is still uncertain, but it causes secretion of estrogen and may act also on the hypothalamus. It will bring about ovulation in 7 out of 10 cases and conception follows in over half of these.

The whole subject of surgical control of fertility and infertility is reviewed by Steptoe. He considers sterilization of the female by a laparotoscope technique sometimes combined with vaginal termination of an existing pregnancy. He also discusses culdoscopic techniques and sterilization of the male. The question whether to sterilize a husband or wife is considered. Steptoe finds it best to interview both parties together, remembering that after sterilizing of the wife, intercourse can be resumed in a week, whereas there is a delay of two months or so before the vasectomized male becomes infertile.

Potts and Sawyer review in detail the effectiveness and risks of methods of contraception control. They point out that there is no generally accepted evidence that oral contraception causes either cancer or fetal abnormalities. We cannot yet distinguish those women at risk from the pill as regards other side effects not due to the pill. Moreover, those who are at greater risk such as diabetics and hypertensives are also at risk if they become pregnant.

While there are no dangers attributed to the older methods of contraception such as coitus interruptus or the provision of mechanical barriers, the same cannot be said of the intrauterine device. Even the rhythm method has been alleged to be responsible for an increased incidence of tubal pregnancy, placenta praevia and malformation, but the evidence is exceedingly slight.

Potts account contains a wealth of information on techniques, side-effects and sequela of induced abortion. Every woman in these circumstances should be offered contraceptive service at once and an IUD can be inserted at the time of operation without increased risk of infection, perforation or expulsion. Oral contraceptives can be started 5 days after abortion.

Two papers look at the difficult and so far impractical subject of interruption of male fertility either by immunological methods (Edwards of Cambridge) or anti-spermatogenic agents (Jackson of Manchester). A third paper by Lacy and Potts considers the significance of the site of hormone production in the mammalian testes from the point of view of fertility control.

Fertility can certainly be impaired by immunological methods. An example are the antibodies to testes tissue or spermatozoa which can disrupt spermatogenesis. In fact circulating and local autoantibodies against spermatozoa occur in some infertile human males or even in some women in whom this effect on fertility is more conjectural. Work has also been done on animals to create antibodies to eggs and embryos, to placenta, to secretion of the male and female reproductive tracts and to various reproductive hormones and enzymes. Edwards explains the hazards of such techniques of contraception although he believes that they may have possibilities.

The problem with anti-spermatogenic drugs is to sterlize the male without incurring the risk of genetic change to his reproductive cells. The final answer is not yet at hand.

L.H.N.

Retirement Can Be A Waste Of Manpower

Every person knows that some slowed up, or somewhat psychotic people ought to be retired at 50 or in fact at any age, while others are still going strong at 85. Clara Barton founded the American Red Cross when she was 84. Tennyson wrote "The Crossing of the Bar" at 83. Michaelangelo was painting some of his great masterpieces when he was 89. Picasso painted remarkable works at 84 and Verdi at 85 composed great music. Viscount Bryce was past 80 when he wrote his Modern Democracies. Kant at 66 wrote his Critique of Pure Reason.

Some able people are now asking why retire perhaps the most important executive in a big company. It will cost much to find a substitute. Also some able and thoughtful men, says Dr. Walter C. Alvarez are asking why impoverish half of our elderly men? Other able economists are asking how long can we afford to keep dismissing millions of our ablest workers.

A move to keep qualified people over 65 working is to prevent them from losing their social security benefits after 65 if they had tried to work. The bill by Rep. John Byrnes (R-Wis) would exempt workers 65 and over from the Social Security payroll tax and thus increase their equity in Social Security rather than penalize them for continuing to work.

It goes without saying that an older person who continues to work saves the government a lot of money in benefit payments in addition to being a contributing member of society. Under present law, the retirement test prevents many individuals who continue to work after age 65 from drawing any Social Security benefits and reduces the benefits of an even greater number.

Rep. Bynes said it is true that an individual who continues to work might increase his benefits he will ultimately draw by substituting higher earnings in a year after 65 for lower earnings in an earlier year. But in most cases earning capacity declines as an individual becomes older and past 65 earnings will not increase their benefits. If we provided people working over 65 with a paid up Social Security account, it would stimulate many of the citizens over 65 to continue to work.

Social Security cash benefits totaled nearly 27 billion in 1969 or 2 billion higher than in 1968. However, receipt of the trust funds which finance benefits exceeded expenditures by more than 5.5 billion in 1969. This could certainly warrant giving Social Security benefits to workers age 65 and over and not penalize a person who continues to work after 65.

L.H.N.

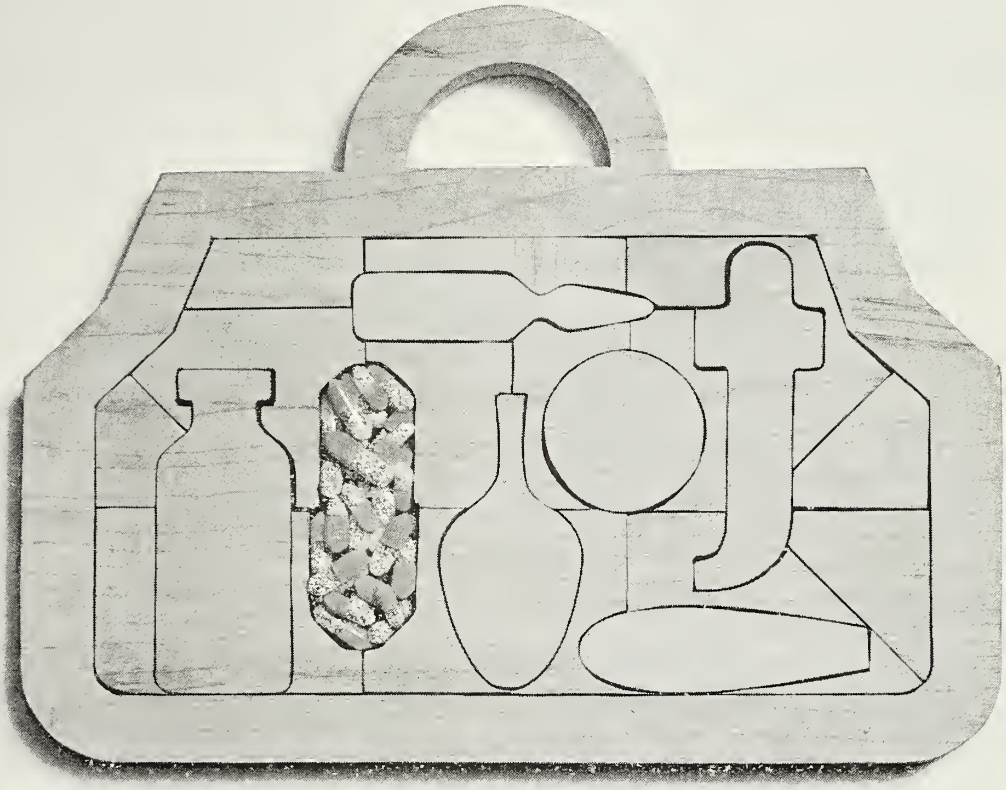
Reference

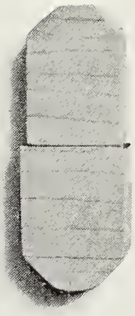
1. Geriatrics, March 1970, p 20.

To Treat Or Not To Treat The Mild Hypertensive

There is not much question about the value of therapy for hypertensive patients with diastolic blood pressure over 110 mg. Hg. Invalidism is reduced, life is prolonged and early complications are lessened. The question remains whether antihypertensive therapy is effective in the patient with mild hypertension, that is the one whose diastolic blood pressure is between 90-100. It must be admitted that there is at present no data available from prospective studies of therapy for the mild hypertensive as there is in the patient with grossly elevated pressure. There is indirect evidence, however, that hypertension is a graded risk and that even mild elevations can be accompanied by increase risk of mortality.

In a recent life insurance study for example there was almost a four fold increase in mortality among men 40-49 years of age whose diastolic blood pressures were between 98-102 mg Hg.





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as compared to normal controls. Data from the Framingham, Massachusetts epidemiological study shows that diastolic pressures greater than 95 mm. in young men are associated with twice the risk of coronary episodes. The mortality among these mild hypertensives is due primarily to hastened atherosclerosis rather than to the complications of vascular necrosis that are associated with deaths among the more severe hypertensives.

Thus putting together a great deal of data we can say that hypertension of any form is a risk and that the specific complications associated with the risk alters with the rise in diastolic pressure. Below 110 mm. Hb. it is primarily an early myocardial infarct or cerebral thrombosis. Above 110 it is heart failure, renal failure and hemorrhagic stroke. In principle the aim of medical therapy is to restore the system to its normal state whenever possible. For example we do not allow our mild diabetics to remain untreated merely because they are mild. They could grow worse untreated. Mild hypertensives can also grow worse untreated either in diastolic pressure or advancing atherosclerosis.

Therapy for the mild hypertensive then is undertaken in the hope of retarding the development of atherosclerosis or progression of the hypertension. In this regard the treatment should be given in conjunction with a general program to control other existing risk factors such as obesity, diabetes, smoking, hypercholesterolemia, gout and other prediseases. The impetus of treatment is greatest in the young, in men more so than in women because of the increased risk of heart disease. In negroes more so than in whites because of the statistically significant increased mortality rate among negro hypertensives.

Currently available mild antihypertensive drugs are accompanied by some side effects, but these the physician can be aware of and control. The prospective studies which will give the physician the definitive answer to the efficacy of such therapy are a decade or more away. In the meanwhile we have patients to see and counsel. We must weigh the risk of antihypertensive therapy in the patient with a mildly elevated diastolic pressure against the risks of not treating him. Is it worthwhile to take a calculated risk based as yet upon admittedly inadequate evidence or relegate the patient to the dangers of hastened atherosclerosis. The physiological physician will elect to bring his patient to as near a normal state as he can, accepting the calculated risks of the drugs used in therapy as the lesser risk of the two alternatives.

Some clinicians are not quite so sure. They point out it is an admittedly mild disease and therapy once begun might have to be continued for a long time. This means any drugs used that long must be non-toxic. The thiazides presently in use can be toxic to some extent and there is a great deal still to be learned about them. They raise the further question of the mental effect on the patient of knowledge that he has a disease he must treat for a lifetime, with medications that are not without risk. Particularly is this important when the evidence is still lacking that the therapy offered will significantly benefit him even if the blood pressure is lowered.

It is a knotty problem and we may be sure of one thing that whatever course the doctor chooses he cannot blame himself if the outcome should be unsatisfactory.

L.H.N.

Reference

1. JAMA, 208: 29, April 7, 1969.

The Heroin Plague

In New York City, among the estimated 100,000 heroin addicts, more than 900 fatalities due to drugs occurred in 1969. In that city, drug abuse is the leading cause of death between the age group of 15 to 35. According to Michael M. Baden, deputy Chief Medical Examiners, the majority of fatalities are due to an acute reaction to the intraveneous injection of a mixture containing heroin. This type of death was dramatically portrayed early this spring when Joseph W. Spellman, Chief Medical Examiner of the City of Philadelphia addressed medical colleagues on the topic of sudden death from heroin. To a shocked audience he showed photographs of victims with needles remaining in their veins who had died after self-administration of drugs.

The mechanisms involved in the deaths are not clearly established. Some investigators consider allergic reactions, while others have suggested overdosage. A survey of the practices attending the production, distribution and usage of heroin leaves one amazed that the death rate is not higher than it is. The method of illicitly extracting morphine from opium is quite crude. The impure morphine is then acetylated to heroin in secret laboratories, mainly in France. This

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product is 90 per cent pure. Subsequently, however, the heroin passes through a complex distribution system and is adulterated repeatedly in unsterile conditions with a variety of additives quinine, mannitol, and other white powders.

During heroin's infancy as an addiction problem here, Dr. Helpern, the Chief Medical Examiner in New York City, uncovered an epidemic of 136 cases of malaria among the patients he autopsied from 1933 to 1943. These malaria cases occurred among heroin addicts who by sharing needles had transmitted the parasitic infection to each other. Addicts and those who prepared the mixture soon learned that quinine was a cure for malaria and began adding it as a diluent of the heroin mixture and this stopped the malaria outbreak in the heroin addict.

The office of the Chief Medical Examiner of New York City analyzed 132 street samples of drugs, all of which supposedly contained heroin. They found that 12 samples contained no heroin at all, and among the remainder, the concentration of the drug ranged from less than 1 to 77 per cent. Variability in the amount of the drug could be responsible for many fatalities. A user accustomed to a low concentration is likely to die from an injection of almost pure heroin.

The hard core addict subjects himself to more than 1000 intravenous injections per year, and they are thus exposed repeatedly to possible antigens in the crude heroin or its adulterants. In addition, the repeated use of unsterile drugs, unsterile equipment, and unsterile technique leads inevitably to human wreckage. Louria and his colleagues have identified the most common medical problem as liver damage arising from hepatitis. Other diseases that are particularly subject to attack include bacterial endocarditis and pneumonia.

Tetanus now a preventable disease has been a complication of narcotic abuses since the first such case was reported in 1876. Most tetanus victims are Harlem females. Because women's veins often are not prominent and therefore, are inaccessible for intravenous injections, females are more often apt to "skin-pap", a practice more likely to produce tetanus-prone-wound than intravenous "mainlining". Among other complications are emboli from veins or heart valves.

Drug abuse which was once predominantly a disease of Harlem, is now a plague that is spreading to the suburbs. Dr. Abelson points out that drug use has been glamorized, while descriptions of the dreadful consequences have been muted. Parents and educators must inform the young of the corpses and of the physical wreckage. Despite warnings some youth are adventurous, will sample the illicit and many will be hooked. The number of addicts is already estimated at 200,000 and the annual cost of this drug is 5 billion.

With so much at stake in lives and money, the nation should increase its effort to curtail drug abuse and to find better ways to rehabilitate the addict. Two relatively new methods seem promising, one is the use of methadone. A second approach is a psychiatric one which emphasizes attitudinal changes and utilizes ex-addicts to give emotional support to addicts who wish to stop.

Further research might well disclose even better methods. This nation should provide the necessary funds to move vigourously against a spreading plague.

L.H.N.

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2. Louria, D. B., Hensle, T., Rose, J.: Ann. Intern Med. *67*, 1, 1967.

3. Walsh, J.: Methadone and Heroin Addiction: Rehabilitation Without a "Cure". Science *168*, 684, 1970.

Adaptations In Astronauts To Interplanetary Space Flights

The success of interplanetary missions depend on adaptation of the astronauts' cardiovascular and respiratory systems to the environment of the capsule and to the acceleration during their launching into space.

For those hours before the launch astronauts breathe 100 percent oxygen. This is a most essential process for removing nitrogen from body tissues, in order to reduce the possibility of decompression sickness during the initial and rapid fall of cabin pressure. In the event of an immediate failure of the system which controls the initial fall in cabin pressurization to 6 pounds per square inch (0.4 kg per sq. cm.), the astronauts would then be protected by their space suits.

The suit is pressurized normally to 0.24 kg. per sq. cm. and under these circumstances the symptoms of decompression sickness may appear. In case of such an emergency, the Mission Control might be persuaded to end the flight, but the immediate response would be to increase the suit pressure to above its usual working level. This would be in the region of 0.35 kg per sq. cm. and is likely to provide relief from mild symptoms of decompression in most instances. If the spaceflight was to continue restoration of cabin pressure would be essential. However, the protection afforded by the suit would provide an effective environment while awaiting re-entry during the first orbit of the earth.

During the launch of an Apollo Spacecraft the astronauts experience acceleration near 4g. This increased gravitational stress passes over the chest and does not have any adverse effect on the circulation to the brain. Many studies have shown that such forces interfere with ventilation and perfusion of the lungs and it has been observed that during acceleration around 4g the oxygen saturation of the blood falls by nearly 20 percent. In effect a mild form of pulmonary atelectasis develops in astronauts breathing 100 per cent oxygen during the launch. This can usually be cleared by forced ventilation.

Once having adapted to these changes in environment, the final adjustment required of the astronauts is weightlessness. Injection into the earth's orbit occurs about 11-12 minutes after blast off and the changes in the cardiovascular system at this time are quite complex and not yet completely understood. One important change is the reduction of blood volume up to 15 per cent because of sequestration of blood into the central vascular blood pools from the legs into the abdomen and thorax.

It is the reduction of circulating blood volume and perhaps other changes such as reduced venomotor tone following prolonged weightlessness which leads to orthostatic hypotension on return to the earth. Thus the astronauts have to contend with possibility of decompression sickness, acceleration, and weightlessness, in the first few minutes of spaceflight.

L.H.N.

Reference

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The Role Of Sympathetic Blockade In The Treatment Of Hyperthyroidism

Hyperthyroidism is accompanied by symptoms. and signs which closely resemble excessive adrenergic activity. When epidural blockade was performed on dogs made hyperthyroid by thyroid feeding, there was inhibition of cardiovascular effects presumably by inhibiting overactivity of the sympathetic nervous systems.[1] The logical inference from such an experiment was to try sympatholytic agents as therapy for thyrotoxicosis in man.

In 1941 spinal blockade[2] actually was used as treatment for severe thyrotoxicosis. Recently reserpine, guanethidine and propranolol have been advocated to achieve the same result. There are now sufficient data to support the efficacy of one or more of these drugs to alleviate tachycardia, arrhythmia, tremor, eyelid retraction and myopathy in hyperthyroidism. Applied locally, guanethidine eye drops reduces eye-lid retraction, but not proptosis. Many less easily quantified manifestations of hyperthyroidism such as restlessness, palpitation, sweating and heat intolerance are quite uniformly lessened by these drugs, although thyroid function itself is unaffected. Some increase in oxygen consumption, intrinsic heart rate and myocardial contractility persists.

Each of the drugs mentioned above has known assets and also liabilities. Reserpine has a central sedative action, desirable in some cases, but also may precipitate serious emotional depression. Like reserpine, guanethidine has a relatively slow onset of action when given orally (about 6 days) and its effects persist for some days after discontinuance of therapy. It may also produce significant postural hypotension. Propranolol induces a selective betaadrenergic blockade. When given orally or intravenously, it has a very rapid short lived action. It does not tend to cause postural hypotension. On the other hand, it can't be used in heart disease when there is possibility of heart failure.

Adrenergic blockade seems justified in thyroid storm when clinical improvement may be dramatic. The method is indicated also in atrial arrhythmias and in those cases where immediate therapy of ^{131}I or thiocarbamates or surgery are obtained. There is also the possibility that lower doses of ^{131}I or thiocarbamates can be used while most of the signs and symptoms are suppressed by sympathetic blockade. This way there may be a lessening risk of hypothyroidism and adverse drug reactions.

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Some like Pimstone[3] believe that propranolol can be curative in some patients. They report 27 patients with hyperthyroidism in which propranolol was the sole therapy and one fourth experienced complete remission at the end of 1-8 months of observation. They suggest that patients that respond fully to propranolol in low doses may not need more definitive therapy.

The final evaluation on use of sympatholytic drugs requires further answers to several questions. What may be the metabolic consequence of long term adrenergic blockade especially on lipid and carbohydrate metabolism. Are there any hazards in blockade of normal cardiovascular and energy mobilizing mechanisms in long continued hypermetabolism. What difference is there in clinical efficiency of reserpine or guanethidine which impairs catecholamine release from that of drugs like propranolol which selectively block betaadrenergic receptors alone. Would combined alpha and beta blockade have advantages over beta blockade alone. Finally, are the incidence of side effects of these drugs greater than those of anti thyroid drugs.

Until more experience is accumulated, Riddle and Schwartz[4] present a tentative plan for use of sympatholytic drugs in hyperthyroidism. They suggest routine use of these agents to supplement standard modes of therapy. Adrenergic blockade alone may have some merit in mild cases or where other forms of therapy are disadvantageous. They report use of guanethidine to prepare a pregnant hyperthyroid woman for surgery. They also report a 19 year old girl resistant to methimazole therapy who is mildly but definitely hyperthyroid after a second subtotal thyroidectomy who obtained relief after 4 months of guanethidine therapy when a complete remission occurred.

As to the selection of drugs, choice usually rests between guanethidine and propranolol. Reserpine has been widely used and is effective but frequent side effects makes it rarely the drug of choice. Guanethidine seems next in long term therapy with a single morning dose. Ptosis and postural hypotension are useful as therapeutic end points. Propranolol is preferable when rapid onset of action is required as in thyroid storm or when quick withdrawal before surgery is desired. Patients with troublesome postural hypotension are also candidates for propranolol. Obviously, as always therapy should be tailored to suit each patient's special needs.

In a few years a more definitive appraisal of the use of these drugs should be possible. As Riddle and Schwartz[4] point out "the classic pattern of use of a new drug is said to include discovery, acclaim, abuse and disrepute before its appropriate place is established". A conservative attitude will help us to avoid the phases of abuse and disrepute in the case of sympatholytic drugs for treating hyperthyroid patients.

L.H.N.

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Recent Progress In Anesthesiology

Improvements continue in the design of anesthetic apparatus for safer and more physiologic conduct of anesthesia[1]. There is now a wide valve device to overcome the problems of dead space and resistance to gas flow. Another is a modification of the gas supply system to limit the maximum concentration of nitrous oxide to 75 per cent. Still another is the introduction of fused monitor cables to reduce hazards from shock and thermal injury from electrical monitoring equipment, external cardiac pacemakers and intravascular catheters. The device can also protect the patient from stray currents when electrocautery is being used. Finally is the prevention of cross infection by using disposable objects which don't need sterilization.

In the fiield of intravenous anesthetic, thiohexital is found to be the most rapidly metabolized barbiturate ever studied in man. For outpatients a short action and rapid recovery from anesthesia was found in Propanidid. Ketamine is another drug but has hallucinatory potential. Each of these new drugs have undesirable side effects which must be overcome

There are new local anesthetic agents. One is prilocaine much less toxic than lidocaine but with a duration of action equivalent to it. Methemoglobin production by this agent depends on the dose used and can be avoided by limiting it to a maximum of 10 mg per kg at any one time. Prilocaine carbonate in epidural anesthesia results in more rapid onset of anesthesia with more intense sensory and motor blockade. Reduced dose requirements would lower toxicity.

Anesthesiologists have been prompt to apply computer techniques for purposes of investigation, teaching, patient care and data processing. Cole et al[2] described a number of teaching applications, including electric analogues of CO_2 distribution, of O_2 stores in the body and an oxygen dissociation-curve generator. Shinosaki et al[3] developed a computer program for nitrogen washout for clinical evaluation of patients with obstructive pulmonary disease, enabling the degree of impairment to be quantified.

A unique contribution to teaching in anesthesiology was devised by Denson and Abrahamson[4]. Their creation is a life-sized model of a man known as "Sim One," a computer-controlled patient simulator capable of demonstrating symptoms and reactions that the trainee in anesthesiology might encounter during an anesthetic and surgical procedure. The supervising instructor can introduce problem situations such as laryngospasm, vomiting, cardiovascular abnormalities and injections of various drugs, to all of which the trainee must respond appropriately.

Also being explored is application of rapid data processing to the care of the anesthetized patient. There are advantages of mechanization of patient monitoring, the cumbersome nature of the currently available hardware tends to restrict its use to specially selected problem situations. Perhaps miniaturization and simplification of the necessary components will lead to a more widespread use in the future. Data processing for storage and retrieval has applications in anesthesia as in other branches of medicine. A recently advocated recording system by Moore et al[5] is permitting ready retrieval of stored information.

Outside the operating room, the anesthesiologist's skills and disciplines are also coming to be required. He has become involved in the pain clinic through his expertise in nerve block with its emphasis on diagnostic and therapeutic nerve-blocking procedures. Similarly his intense commitment to the postoperative recovery room is being equally and logically extended to problems in the development and management of intensive-care units, services for inhalational or respiratory therapy and emergency resuscitation teams.

In some hospitals fluid therapy in its protean aspects has become the province of the anesthesiologist. At least one is director of a regional blood bank and another department of anesthesiology has been charged with operation of artificial-kidney units in its institution. Historically, specialized units for prolonged care of the comatose or otherwise seriously impaired patient have tended to become the province of the physician who first dedicated himself to the solution of the presenting problem, regardless of his own field of specialization, whether internal medicine, neurology, psychiatry or anesthesiology.

Management of such units with the possible exception of the CCU is now more commonly assumed by or even thrust upon the anesthesiologist. Obviously, for the operation to be successful, one needs frequent collaboration with specialists in many areas, regardless of which one is actually in charge.

L.H.N.

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Cross Reactions Of Oncogenic Viruses

A working conference was held on August 28-29 sponsored by the Immunology-Epidemiology segment of the Special Virus-Cancer Program of the National Cancer Institute. Information was presented on the C-type leukemia and sarcoma viruses and on herpesviruses suspected of being oncogenic.

On the first day the speakers discussed the antigens of the viruses that are associated with leukemia and sarcoma in chickens, mice, and cats, as well as the antigens of the C-type particles associated with certain leukemias and sarcomas in man. The finding that some human tumors contain a common antigen suggested that some of these malignancies may be viral in origin. C-type virus particles have been seen on electron microscope examination and after culture of cells from human osteosarcomas and liposarcomas. The C-type particles have also been found in plasma sediments of patients with various leukemias. Serum of patients seemed to possess antibodies which normal individuals did not possess.

There was also much discussion on cross reactions between oncogenic viruses of man and other species. Many of the participants described attempts to find human serum antibodies to the various oncogenic C-type viruses isolated from different animal species. Some human serums apparently neutralize avian and murine viruses. However, most of the results were negative. Such studies should be pursued until an unequivocal answer is obtained.

On the second day the speakers discussed several types of herpes viruses which have been associated with various malignant states of animals and man. These viruses are not always present in malignant cells in viro, but often appear in cultures of these cells. This raised the question whether they are passengers or tumor producing viruses. Two human strains of viruses were discussed, one from Burkett's lymphoma and one believed to be associated with cervical carcinoma (Herpes hominis II.). Three animal virus strains were also considered.

Immunological studies on the relatedness of these tumor associated viruses were reported from two different laboratories. Initial attempts to determine common antigens among the various viruses and one herpes virus from Marek's disease (chicken lymphoma) have so far been negative perhaps because of insufficient viral mass. A detailed report showing the high association of antibodies to H. hominis II in the serums of women with cervical cancer was presented.

Important new findings on herpes virus associated with Marek's were presented. The evidence indicates that this virus is probably etiologically related to the disease. First is that a herpes virus has been isolated from every strain of chicken with Marek's disease. Second is that the growth rate of herpes virus is similar both in vivo and in vitro. The third argument is that fluorescent antibody foci are observed early in tissue culture and later progress to cytopathic areas with virus demonstrable by electron microscope. The disease can be transmitted to normal chickens by virus found in the cells

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Side Effects include drowsiness, usually transient, if persistent and associated with ataxia, usually responds to dose reduction, occasionally concomitant CNS stimulants (amphetamine, mephentermine sulfate) are desirable. Allergic or idiosyncratic reactions are rare, but such reactions, sometimes severe, can develop in patients receiving only 1 to 4 doses who have had no previous contact with meprobamate Previous history of allergy may or may not be related to incidence of reactions Mild reactions are characterized by itchy urticarial or erythematous maculopapular rash, generalized or confined to groin Acute nonthrombocytopenic purpura with cutaneous petechiae, ecchymoses, peripheral edema and fever have been reported. One fatal case of bullous dermatitis following intermittent use of meprobamate with prednisolone has been reported. If allergic reaction occurs, meprobamate should be stopped and not reinstituted Severe reactions, observed very rarely, include angioneurotic edema, bronchial spasms, fever, fainting spells, hypotensive crises (1 fatal case), anaphylaxis, stomatitis and proctitis (1 case) and hyperthermia. Treat symptomatically as with epinephrine, antihistamine and possibly hydrocortisone. Aplastic anemia (1 fatal case), thrombocytopenic purpura, agranulocytosis and hemolytic anemia have occurred rarely, almost always in presence of known toxic agents. A few cases of leukopenia, usually transient, have been reported on continuous administration.

Meprobamate may sometimes precipitate grand mal attacks in patients susceptible to both grand and petit mal. Extremely large doses can produce rhythmic fast activity in the cortical pattern. Impairment of accommodation and visual acuity has been reported rarely After excessive dosage for weeks or months, withdraw gradually (1 or 2 weeks) to avoid recurrence of pretreatment symptoms (insomnia, severe anxiety, anorexia). Abrupt discontinuance of excessive doses has sometimes resulted in vomiting, ataxia, tremors, muscle twitching and epileptiform seizures. Prescribe very cautiously and in small amounts for patients with suicidal tendencies Suicidal attempts have resulted in coma, shock, vasomotor and respiratory collapse and anuria. Excessive doses have resulted in prompt sleep, reduction of blood pressure, pulse and respiratory rates to basal levels; and occasionally hyperventilation. Treat with immediate gastric lavage and appropriate symptomatic therapy. (CNS stimulants and pressor amines as indicated). Doses above 2400 mg./day are not recommended.

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lining the feather follicles of infected birds and the virus can be reisolated again from infected birds. The final point made was that protection can be obtained in chickens by inoculation of a live but apparently non-pathogenic strain of herpes virus of turkey origin.

If it is possible to produce immunity against oncogenic viruses and prevent cancer from this source, then we are at the threshold of a new era in cancer prevention.

L.H.N.

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A British Clinician Speaks

Dr. X in his late 30's has been a consultant internist for 5 years. He has two consultant colleagues working in the hospital each with 30 beds. He likes the county in which the hospital is placed although the community is relatively poor. His connection with the teaching hospital ensures that his residents are the best graduates of the year. The quality of his juniors have been high although once passed by the Boards, they scuttle back to their teaching hospital. All attempts of persuading the new school to start a scheme of rotating interns and residents have so far come to nothing.

Dr. X does 2 ward rounds and 2 other sessions a week in this hospital and another 5 outpatients at various local hospitals. Officially he is on one night and weekend in 3, but actually he is being phoned up and can't retire before 12. In other words, he is overworked. Then, there are the committee meetings and house calls. He has 2 private consulting sessions a week in town, but the county is poor and there is not much demand for private practice.

A merit award is a real prize but he points to some who get it because of acquaintance higher up. He spends 4 hours a week at clinical meetings or teaching, postgraduate teaching is flourishing. He teaches medical students attached to his hospital in the summer and is also obliged to lecture to nurses. But study leave and travel grants to juniors to go to conferences results in little time left for reading journals, doing any research, or seeing his family.

The hospital itself has good points, a really modern purpose built well, attractively designed both inside and out with a superb view of the country-side from its windows, first rate ancillary diagnostic facilities, modern equipment and well-trained nurses. But it is far too small, first planned 15 years ago, took 5 years to build and nothing new is expected for 10 years.

At present he is working under great pressure, he saw 6500 outpatients last year and 1300 went to the hospital. This year the work load is up 20 per cent. He thinks the patients are definitely adversely affected by this pressure. He had to discharge a suspected coronary prematurely who died at home 2 days later of left ventricular failure. There is a shortage of equipment, for example only 4 monitors on six patients. In a recent flu epidemic, there were not enough respirators to treat all the patients seriously ill with pneumonia so that probably some died "whom we could otherwise have saved".

The solution to many of these problems was, of course, more money for geriatric beds to start a thorough going progressive patient care system, to have more nurses, to pay secretaries better to avoid attraction by higher wages in town. Money was needed for a crash building program to provide another 60 beds and to enable another consultant to be appointed. The competition from private practice was small and if his salary could be raised to 6000 pounds, he would willingly transfer to full-time and spend more time in the hospital.

Another consultant would also help to cover for emergencies and off duty periods. Now to attend courses in advanced medicine it means the third consultant carries an extremely heavy burden during the week. They have tried to get general practitioners to work in the hospital, but they usually say they are too busy or not interested as the pay is not enough.

To raise the extra money needed would require more money to be spent in health. They could cut down on travelling distances to make house calls and centralize the outpatient clinics from an area of 12 miles. But this would impose a real burden on patients and so they accept the excess burden in the interest of the patient. He thinks there is too much bureaucracy and too little dialogue between "higher ups" and themselves. Decisions are made higher-up by people who have no knowledge of how the consultants work, what they need. Furthermore, higher-up decisions take interminably up to 2 years.

The good and bad aspects of the set up was stated very clearly by Dr. X. He agreed he was practicing the kind of medicine he wanted to without clinical interference and that he would not change his job for anything. However, he thought that compared with the local general practitioners and other professional men, the consultants were poorly paid for the long hours they worked, especially the clinicians.

What really irked him was the meanness of the authorities. No realistic payment was made for the many hours spent travelling to and from outpatients and home visits. No proper time allowance was made for the periods spent dictating letters and notes, administration and teaching. The refusal to pay for any more than 200 house visits a year, was grossly unfair, since they had to be made often at inconvenient hours and in his spare time.

What really worried Dr. X was what the position would be in 15 years. He doubted whether working conditions would get better and in fact saw objective signs that they were deteriorating. "I know many people might envy one this new hospital", he said because as registrars they were conditioned to work in 19th century conditions. In fact one kind of place should be what we and the patients expect as a right as they do in Scandinavia.

He was sure the present situation would be changed, but he thought in his region they're going about it the wrong way. They are trying to build 5 district new hospitals without the expertize or resources. I've seen the existing slums at I J & K and I don't blame anybody for agitating for their replacement. But surely he thought it would be better to concentrate on setting up one really first class complete unit in one place and with this experience, move on to the next. L.H.N.

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Carbon Monoxide And Atherosclerosis

For a long time nicotine in tobacco smoke was considered to be the active agent in the development of atherosclerosis, whereas carbon monoxide (CO) in the tobacco smoke was not given any pathogenetic importance. In animal experiments nicotine has shown no atherogenic effects. On the other hand when cholesterol fed rabbits were exposed for 8-10 weeks to enough CO to lead to a COHb concentration of 15 percent, atheromatosis was greatly enhanced. The amount of cholesterol in the aortic wall of the experimental animals was on an average 2.5 times higher than in the control animals also fed cholesterol but not exposed to CO. Even non cholesterol fed rabbits exposed to CO (11% COHb) for 12 weeks also developed arterial lesions. Such high concentrations of COHb have also been found in smokers who have early peripheral or coronary atherosclerosis.

The arterial lesions of the experiment rabbits were indistinguishable from lesions produced by prolonged exposure to arterial hypoxia—10% O2 in nitrogen in insperatory air. The cholesterol concentration was on an average 3.5 times higher in the exposed cholesterol fed rabbits than in control rabbits breathing atmospheric oxygen. Hyperoxia, 28 per cent in inspiratory air—on the other hand held the lipid accumulation in aortic walls of cholesterol fed rabbits to half the values of controls.

In each hypoxia type of exposure whether it was due to CO or reduced oxygen tension the microsocopic changes in the vessel walls were identical. There was endothelial hypertrophy and proliferation. There was splitting up of the subintimal structure and marked focal subintimal edema. When the exposed rabbits were also fed cholesterol a marked lipid accumulation occurred with formation of a plaque. In addition the hearts showed also degenerative myocardial changes. In the experimental production of atherosclerosis we see the interaction between an injured intima and increased lipid concentration of the blood. The medical importance of this theory is that it can explain atherosclerosis from a wide variety of known risk factors. It certainly helps understand the atherogenic action of carbon monoxide which in the form of COHb is frequently elevated in cigarette smokers.

Attention has not been paid earlier to vascular changes caused by chronic CO exposure giving only moderate COHb concentrations. The biological mechanisms involved in the hypoxic production of vessel injuries are still not clear, but could be a consequence of increased permeability of the endothelial and mesothelial membrance caused by CO. This view is supported by frequent presence of abnormal fluid accumulation in the serous cavities of many of the CO exposed animals. The localized edema in the aorta probably reflects a disturbance in the transport of fluid across the arterial wall. Increased vascular permeability for albumin and lipoprotein increased capillary filtration in human subjects after moderate exposure to CO[1] in human subjects certainly suggest that the subintimal edema is due to altered permeability.

It would appear that oxygen demanding systems are necessary to maintain the integrity of the endothelial part of the arterial wall. CO and hypoxia damages these systems and results in transfer of elements from the ambient blood into the subendothelial spaces at a rate faster than they can be disposed of. If the blood is also altered by increased amounts of large lipoprotein molecules, more will enter the subendothelial space than can be removed. Chances for production of a plaque increases.

The atherogenic effects of low concentrations of COHb might be related to several medical problems. The increased risk of arterial disease among smokers will now be studied prospectively by estimating its association with COHb levels. If the results of such studies confirm a role of CO in the development of atherosclerosis in man, they will, of course, be of interest from a preventive point of view concerning all types of exposure of man to this toxic gas.

Furthermore, a proved atherogenic effect of CO exposure will be of great interest for atherosclerosis research. It may clarify current views on the causes and pathogenesis of the disease, especially the views concerning a relation between induced permeability change and the filtration of lipoproteins into the arterial wall. These studies have furnished strong support to Professor Levin Waters' view of atherosclerosis propounded some years ago in which an experimentally damaged intima by allylamide together with high concentrations of lipoproteins caused the atherosclerosis plaque to develop.

If one views atherosclerosis as a disease of arteries caused by a damaged intima and increased lipoproteins in blood, it helps to bring some order out of the diverse "risk" factors already established as being related to atherosclerosis. L.H.N.

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THE COVER

"The incidence of cancer in Connecticut residents continued to rise steadily in 1966." So summarize Barbara W. Christine, M.D., M.P.H., Chief, Chronic Disease Section of the state health department, Research Analyst Paul D. Sullivan and Biostatistician Roger R. Connelly in an article, "Cancer in Connecticut, 1966", published in the May issue of the *Connecticut Health Bulletin.*

Cancer continues to be one of the two leading health problems. It is the second leading cause of death in Connecticut, as in the entire nation, accounting for 169 deaths per 100,000 persons in 1968 as compared to 354 due to heart disease.

A total of 8,942 cases of cancer were diagnosed among Connecticut residents in 1966. Though the greatest incidence occurred in the older age groups, over half the cases were under the age of 65 and one in five was less than 50 years of age. *As in each year since 1949, cancer was more frequently reported in men than women.*

Lung cancer, in which cigarette smoking is implicated as a cause, is continuing its sharp increase in *men,* making this their most common tumor. Though lung tumors are increasing in *women* as well, the rate is only one sixth that of men.

The most frequent tumor diagnosed in Connecticut *women* is *breast cancer* accounting for 27 percent of their tumors.

Cancer of the *cervix of the uterus* rose from 32 per 100,000 in 1960-1964 to 39 in 1966. Yet all of this increase represented tumors in the early noninvasive stage, reflecting increasing use of Pap tests which enable physicians to detect cancer in its most easily curable stage. There was a concomitant decrease in the more advanced invasive tumors of the cervix. Tumors of the body of the uterus, however, increased slightly.

The incidence of cancers of the *male genital system* changed little from the 1960-1964 period to 1966, while rates for tumors of the *urinary organs* increased in *men,* a rise not seen in *women. Cancers of the mouth, throat and of the lumphatics and hematopoietic* tissue occurred more *frequently in men* than in *women.*

The impact of cancer on an individual in terms of the threat it represents to the normal life span depends on such factors as the type of the tumor, early diagnosis and promptness of treatment.

In 1966 cancers of the digestive tract and lung, bronchus and trachea accounted for approximately half of all cancers in men, while tumors of the breast and reproductive organs accounted for a similar proportion in women.

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Hereditary Pancellular Lysosomal Gigantism (Chediak-Higashi Syndrome)

Case Report

Frederick J. Flynn, Jr., M.D., Mary S. Coley, M.D.,
Ronald S. Beckett, M.D., and B. Shannon Danes, M.D.

The Chediak-Higashi syndrome is now considered one of an increasing number of diseases associated with lysosome dysfunction. Many of the inflammatory and storage diseases of childhood are believed to be related to malfunction of the "many-faceted lysosome." The inclusion bodies or giant lysosomes seen in the leukocyte are good cell markers but it must be recognized that all cells are involved in this disease process.

Hereditary lysosomal gigantism, first reported by Bequez Cesar in 1943,[1] later by Chediak in 1952,[2] and Higashi in 1954,[3] is an uncommon familial condition. Thirty-three cases had been reported by 1964 when Kritzler reviewed the condition.[4] Clinical manifestations include partial ocular cutaneous albinism, frequent infections, neuropathies, occasional mental retardation, hemorrhages, and often terminal lyphoma or leukemia.[5] Inheritance is autosomal recessive.[6] Peripheral leukocytes contain large cytoplasmic granules pathognomonic for this condition.[7-9] These have been demonstrated by electron microscopy to be giant abnormal lysosomes.[10, 11] The hypopigmentation of hair, skin, and retinae is postulated to result from abnormal packaging of normal melanosomes in the epidermal cells.[12] Massive cytoplasmic particles similar to lysosomes have been demonstrated in Schwann cells of a peripheral nerve biopsy in a patient with Chediak-Higashi syndrome and clinical peripheral neuropathy.[13] Also, cytoplasmic inclusions have been demonstrated in many cells of neuroectodermal origin, capillary endothelium, and renal tubular epithelium.[14] Recent studies of granulocyte metabolism suggest the peripheral granulocytopenia of this syndrome results from increased intramedullary destruction of granulocytes by the process of autophagia.[15, 16] During this process, small lysosomes fuse to form the well-known large lysosomes. Hypersplenism contributes to granulocytopenia.

Report of A Case

N. C., a twelve-year-old pubertal girl, was admitted to Hartford Hospital in October 1965 with a two-week history of scarlatina-like rash, stomatitis, conjunctivitis, delirium and ankle edema. The pertinent physical findings were fair skin, retinal albinism, absence of palpable liver and spleen, hypoactive deep tendon reflexes, lower extremity weakness, and a normal sensory examination. Past history revealed low normal intellect, intolerance of sunlight since infancy, and excessive bleeding following excision of a mole at eight years of age. The diagnosis of Chediak-Higashi syndrome was made on the basis of the inclusion bodies present in the peripheral smear (Fig. 1) and bone marrow (Fig. 2).

The parenteral administration of albumin temporarily relieved the generalized edema and delirum which were attributed, at least partially, to the low serum albumin (Table 1). Within two months there developed splenic enlargement, generalized edema and ascites, and marked hyperesthesia of the lower extremities. Later weakness of the arms and shoulders developed. Oral and gingival bleeding occurred. Hematological workup revealed abnormalities in prothrombin consumption, platelet counts, and bleeding time. Bleeding ceased with the administration of fresh blood tranfusions and Vitamin K. During the next ten-month period, there were three episodes of hyperesthesia and

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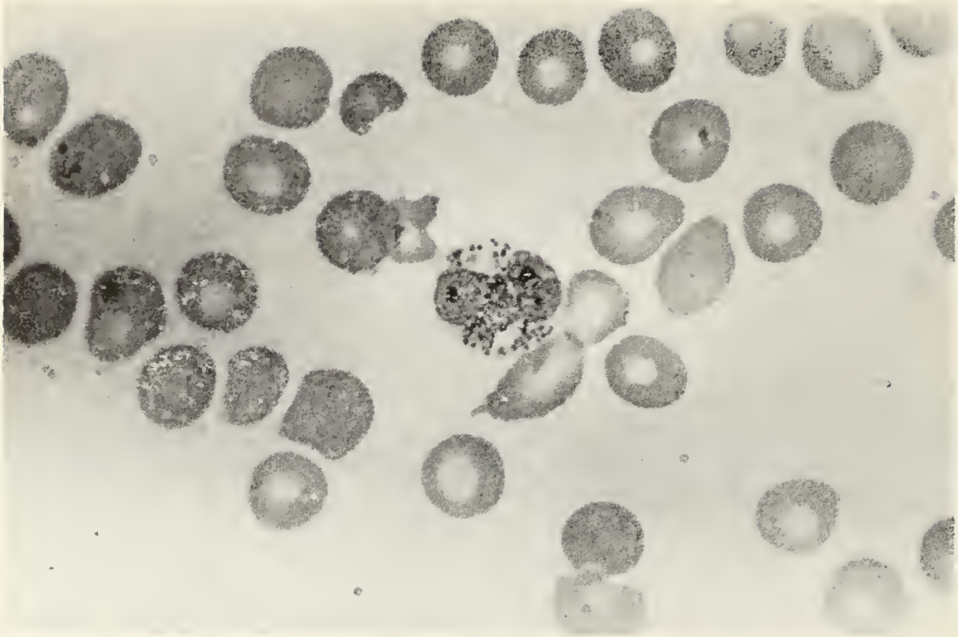

Figure 1
Peripheral blood smear showing inclusions in polymorphonuclear leukocyte.

TABLE 1

SERUM PROTEIN ELECTROPHORESIS. FIRST ADMISSION.

TOTAL SERUM PROTEIN	5.5 g
Albumin	1.9 g (N 2.8-3.9 g/100 ml)
Alpha I	0.3 g (0.4-0.8 g/100 ml)
Alpha II	0.7 g (0.7-1.5 g/100 ml)
Beta	0.8 g (0.7-1.4 g/100 ml)
Gamma	1.8 g (1.0-1.9 g/100 ml)

severe pain of the extremities, relieved by bed rest and protection from ultraviolet light during hospitalization. There was associated gradual loss of the sensory modalities of pain, position sense, and vibration. Concomitantly, severe intentional tremor and bilateral foot drop developed.

A moderate remission occurred twelve months after onset, during which time the patient became

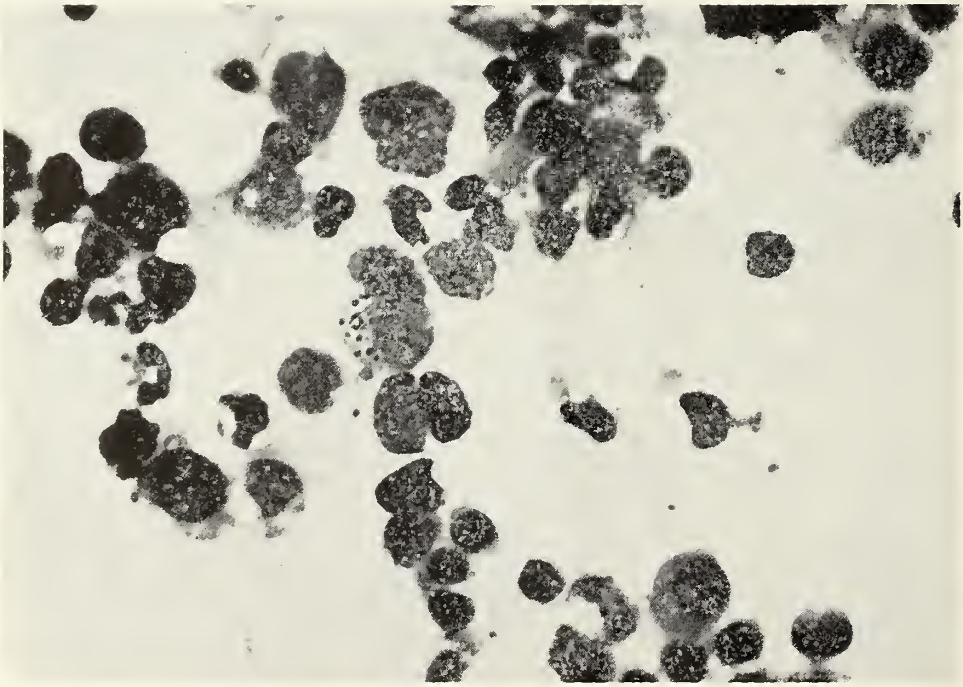

Figure 2
Bone marrow showing inclusion bodies in mononuclear cells.

ambulatory with short leg braces and crutches, and again attended school.

The final exacerbation came twenty months after onset and was manifest clinically in three ways. There was further deterioration of the peripheral nervous system, as noted by increasing sensory loss progressing to anesthesia, motor power loss progressing to total flaccid paraplegia, and urinary incontinence. Electrolyte imbalance developed with hyponatremia resistant to treatment. A second hemorrhage (severe) occurred, caused by afibrinogenemia (Table 2). Prednisone in large dosage was instituted because of reports that corticosteroids reduced the permeability of the lysosomal membrane.[17] Hemorrhagic manifestation subsided within twelve days. The serum sodium returned to normal, but serum albumin level remained low. Search for the site of protein loss was non-productive. A third hemorrhage (massive) from the large bowel was successfully treated with whole blood, plasma, fibrinogen, and epsilon amino caproic acid* without benefit of laboratory studies because of the fulminant nature of the process. High dosage Prednisone was continued. The spleen returned to normal size. The flaccid quadriplegia remained. Coagulation studies returned to normal and the neutropenia improved. Two months later there was a two-day episode of hematemesis without evidence of coagulation defects. Fibrinogen level, prothrombin time, partial thromboplastin time, and platelet counts were all within normal limits. Aspiration, atelectasis, and terminal pneumonitis caused her demise two years from onset of clinical disease.

TABLE 2

CLOTTING SURVEY

Quick Prothrombin Time	28/12 sec.
Ware and Quick Prothrombin Time	30/20 sec.
P.T.T.	81/29 sec.
Thrombin Time	Infinity
Factor VIII	50%
Factor IX	25%
Fibrinogen Assay	0

TABLE 3

LIPIDS (SERUM)

TOTAL LIPID FAT ACID (N = 200-400)	304 mgm%
Phospholipid (N = 100-200)	144 mgm%
TOTAL CHOLESTEROL (N = 150-250)	65 mgm%
Free Cholesterol (N = 70-75)	4 mgm%
Neutral Fats (N > 100)	200 mgm%

Significant laboratory data during this two-year period were as follows: persistent neutropenia, elevated spinal fluid protein, abnormal liver function tests (cephalin flocculation, thymol turbidity, SGOT, SGPT, serum cholinesterase). The fat and protein studies are shown in Tables 1 and 3.

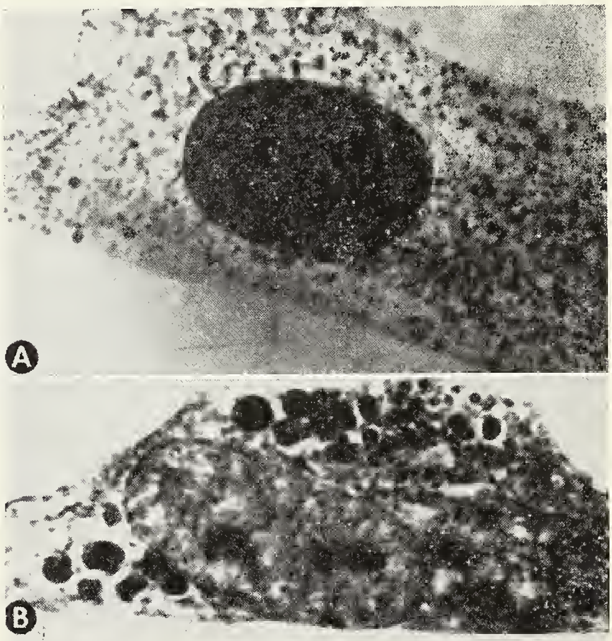

Figure 3

Skin fibroblasts grown in cell culture. Preparations fixed in methanol and stained with toluidine blue O. (A) Fibroblast from normal control (X 5000). (B) Fibroblast from patient (N.C.) with Chediak-Higashi syndrome (X 5000). Inclusions of various sizes and shapes distributed throughout the cytoplasm.

Genetic Studies

Skin fibroblasts, from the patient and her parents, grown in tissue cell culture contained the abnormal cytoplasmic inclusions seen in the peripheral leukocytes of this patient and others with this diagnosis.[18] Cultures of the patient's fibroblasts revealed inclusions in one month; the parents' cultures were positive in two to three months. Subsequent skin biopsies from nine additional members of the family (Fig. 4) were cultured and cell lines established. Cytoplasmic inclusions were observed in only one cell line (a paternal aunt) indicating a heterozygote. The cell line derived from the maternal grandmother revealed no abnormal inclusions. It was, therefore, presumed that the deceased maternal grandfather was the heterozygote. The paternal grandparents were unavailable for study.[19] Subsequent cell cultures of the patient's fibroblasts showed increased cytoplasmic granulation with in-

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* AMICAR ® Lederle

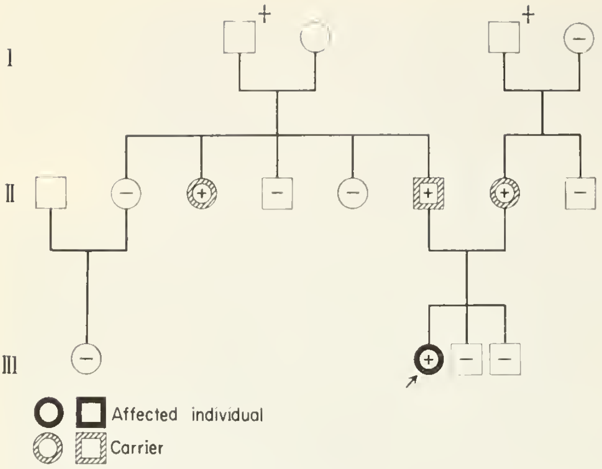

Figure 4

Pedigree of patient (N.C.) with Chediak-Higashi syndrome (autosomal recessive). The signs (positive and negative) inside the square (male) and circle (female) indicate whether skin fibroblasts in cell culture showed abnormal cytoplasmic inclusions.

creased exposure to ultraviolet light and absent granulations in cells grown in virtual darkness.[19]

Pathological Findings

For purposes of comparison, the pathological findings are noted as in a recent comparative pathological report of Chediak-Higashi syndrome in children, cattle, and mink[20] (Figs. 5 through 8): (A) leukocytic infiltration of brain, nerve roots, peripheral nerves, voluntary muscles, posterior pituitary, liver, breasts, smooth muscle of gastrointestinal tract, lungs, and venous walls; (B) cytoplasmic cellular inclusions in leukocytes, anterior horn cells of spinal cord, ganglion cells of inferior olivary nucleus and lateral geniculate body, and renal tubular epithelium; (C) decubitus ulcers, infected phlebotomy, and cut-down sites in the antecubital fossae; (D) partial albinism; (E) vegetative endocarditis (tricuspid valve); (F) focal penumonitis due to Klebsiella pneumoniae; (G) pulmonary fat emboli (marrow and fatty tissue); and (H) superficial gastric and esophageal erosions (gastrointestinal bleeding, clinically).

Discussion

In the sixteen years from 1943 to 1969, a rare, recessively-inherited disease of man has been described in increasing depth. The original diagnostic marker (the giant cytoplasmic inclusion body of the leukocyte) has been found in multiple cell types, correlating to some extent clinical disease with the pathological findings. The technique of tissue cell culture has been utilized in this patient's family to demonstrate the heterozygote. The cytoplasmic inclusion body has been identified as a lysosome and its membrane has been implicated, but not proven, as the source of the defect. Steroids have been noted to be one of the lysosomal stabilizing factors in vivo and in vitro,[17, 21] and did cause

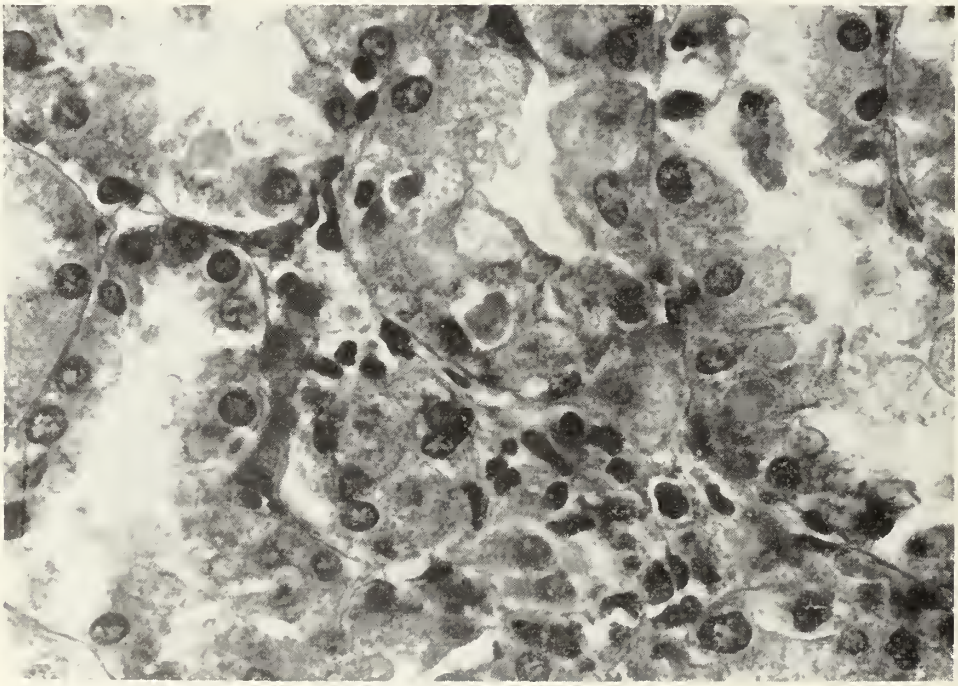

Figure 5

Proximal convuluted tubules containing inclusions (X 430).

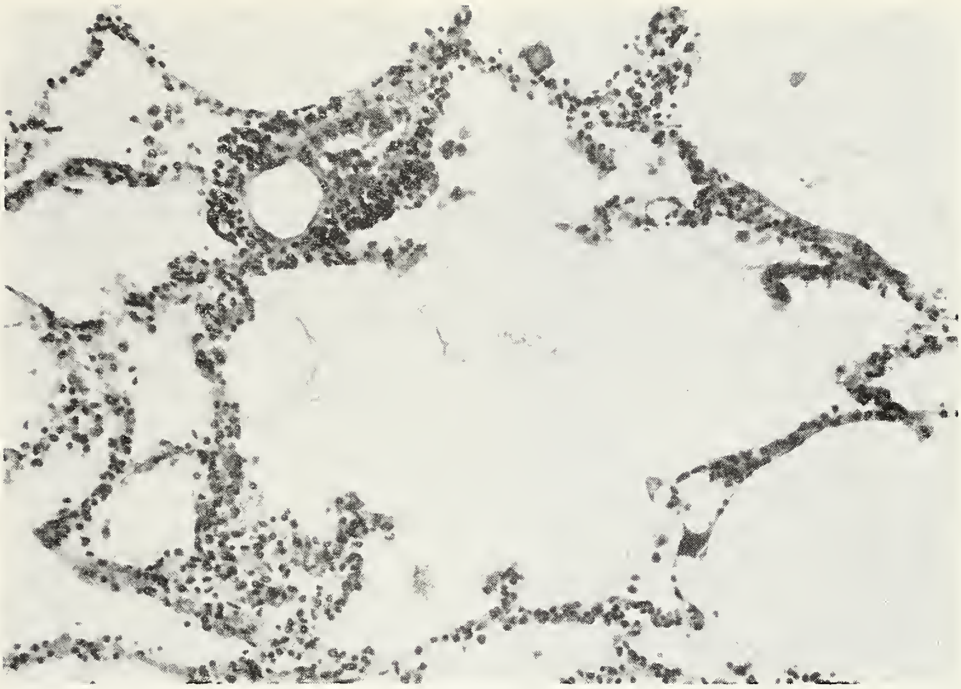

Figure 6

Lung showing fat emboli in pulmonary capillaries on transverse and longitudinal section (H & E, X 100).

temporary amelioration of signs attributed to the leukocyte (decreased splenomegaly and decreased neutropenia) in our patient and others.[16] However, neurological function was not affected by steroids at all in our patient.

Ultraviolet radiation is one of many known lysosomal unstabilizing factors in vivo and in vitro.[17, 20] Our patient's peripheral neuropathy was symptomatically improved (decreased hyperesthesia) and objectively improved (motor strength) when artificial

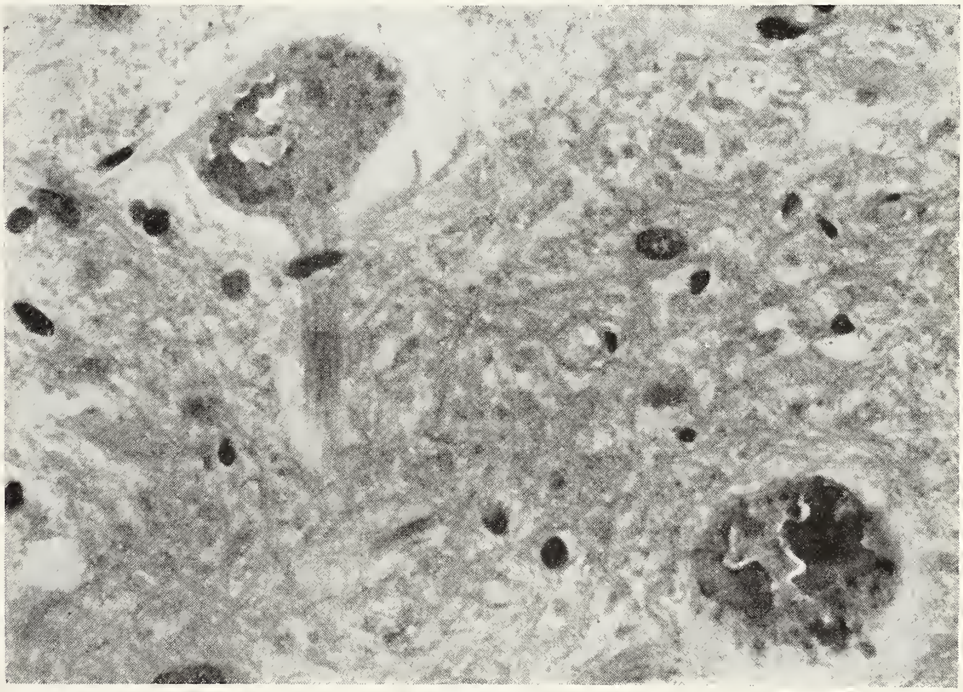

Figure 7

Anterior horn cells of spinal cord showing large irregular inclusions (H & E, X 430).

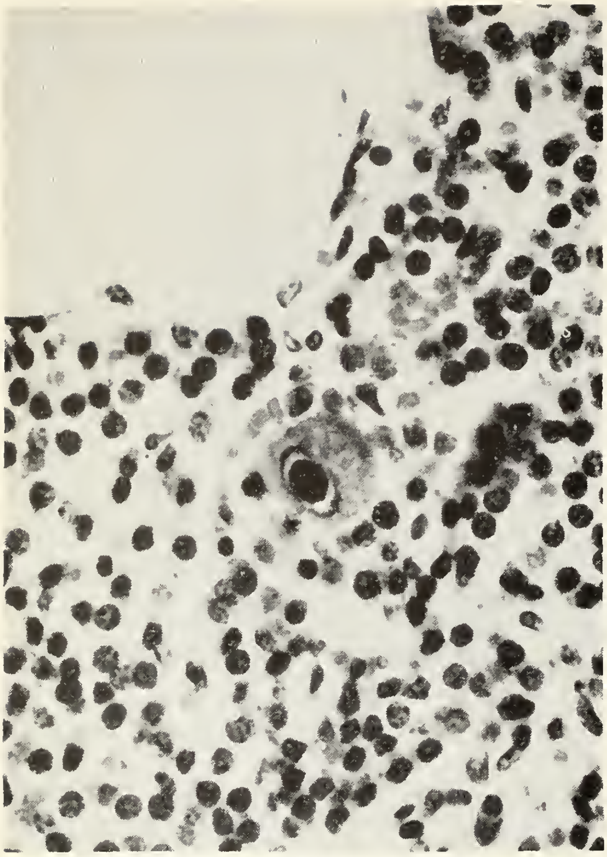

Figure 8

Parathyroid gland showing single cytomegalic inclusion body (H & E, X 430).

and natural daylight were removed as much as possible. The in vitro effect of ultraviolet light was demonstrated by the increase in cytoplasmic inclusions with exposure to light of the patient's fibroblast cultures.[21] Cell cultures grown in the absence of light revealed no inclusions. The persistent low serum albumin and hyponatremia of our patient may be attributable to renal or peripheral tissue damage. The hemorrhagic episodes, caused in part by absent fibrinogen, were undoubtedly contributed to by other factors.

Unexplained is the relatively protracted course of our patient's disease with demise at a later age from hemorrhage and infection rather than lymphoma or leukemia, as has been noted in younger patients. Much remains to know of lysosomal function, possible enzyme defects in Chediak-Higashi syndrome, and the relationship between this human entity and that of mink and cattle.

Summary and Abstract

This is a single case report of a pubertal white girl with Chediak-Higashi syndrome, diagnosed by the stigmata of partial oculocutaneous albinism, frequent infections, and leukocyte cytoplasmic inclusions. Fibroblast tissue cell cultures of the patient and her family documented the homozygous recessive nature of the inheritance. The two-year clinical course was intermittently progressive, with hepatosplenomegaly, peripheral neuropathy, marked peripheral edema, multiple infections and hemorrhages. Supportive therapy prolonged the course. Steroids decreased the splenomegaly and neutropenia temporarily. The peripheral neuropathy improved coincident with the removal of ultraviolet light from the patient's environment. The postmortem findings were consistent with clinical diagnosis.

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OPINIONS ON BREAST CANCER

In summing up a Symposium on Early Carcinoma of the Breast given by the Association of Surgeons at the Annual Meeting in Liverpool in April, 1963, Professor Hedley Atkins first drew attention to the gravity of this situation and reminded the Conference that the figures in the tables and the plots on the graphs that they had been seeing, each represented a human problem, leading at best to a grave disruption of family life and at worst to the loss of a wife or mother in the prime of life.

There was a very wide spectrum of opinion as to how early cancer of the breast could best be treated. This spectrum ranged from those who claimed that any interference with the breast or its lesion, if it had an effect on survival, had a harmful effect, through those who considered it had little or no effect, to those who did increasingly more radical surgical procedures, culminating at the other end of the spectrum with those who, in addition to performing a radical mastectomy with dissection of the internal mammary chain . . . . performed an osteotomy of the clavicle, a dissection of the ipsilateral supraclavicular glands, and a simple mastectomy on the other side.

Professor Atkins emphasized that nobody in this Conference, nor, indeed, anywhere in the world, knew what the correct treatment was within this wide range of possibilities. . . . It was right that surgeons should be dissatisfied with the relatively poor results of the orthodox methods of treatment, but deviation from these methods should be practised only by those . . . . who had an opportunity for studying large numbers of such cases and who could so organize their follow-up that their results would contribute to knowledge and survival might not be unnecessarily prejudiced. . . . The wise course for the practising surgeon, who is not in a position properly to evaluate the many possibilities open to him, would be to treat each patient as a special problem, giving consideration to the nature and size of the lesion and the age and circumstances of the patient. Nevertheless, he (Atkins) was convinced that at this stage the sheet-anchor of treatment of those cases for such surgeons was the operation of radical mastectomy. This operation had a reasonable pathological basis, and, without evidence to the contrary, appeared the most sensible course to pursue.

He believed that Dr. Warren Cole had made a good case for giving synoperative cytotoxins in order to control the isolated cancer cells liable to be set free in the blood-stream as a result of the operative manipulations.—Symposium on Early Carcinoma of the Breast, *Brit. J. Surg.* 51: 226 (March) 1964.

Cancer Incidence, Mortality and Survival In Connecticut During The 1960's

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Roger R. Connelly, M.Sc. and Franklin M. Foote, M.D., Dr. P.H.

Introduction

The Connecticut Tumor Registry is a population-based registry encompassing all cases of cancer diagnosed among Connecticut residents admitted to hospitals.

Ninety-seven percent of the cases registered for 1965 were hospital-reported (Table 1). The remainder of the cases were brought to the attention of the Registry as a result of cancer being mentioned on the death certificates of Connecticut residents dying in 1965. Using these data, the Registry staff is able to calculate incidence and mortality rates as well as survival rates for Connecticut residents.[1-4]

Incidence and Mortality

All Sites

There were 8,665 cases of cancer diagnosed among Connecticut residents in 1965, 4,228 males and 4,437 females (Table 2). The crude incidence rates per 100,000 for each sex were similar, 305.4 for males and 308.0 for females. In 1964, the crude rates were 300.1 and 304.9, respectively.

The age-adjusted incidence rate per 100,000 among males in 1965 was 294.1 (Table 3). This was 5.2 points higher than the rate of 288.9 in the period 1960-1964. The age-adjusted rate for females was 273.4 in 1965. This was 10.7 points above the level in the 1960-1964 diagnosis period, 262.7. The increase for females from 1960-1964 to 1965 was statistically significant ($p < .03$).

References to incidence and mortality rates in the remainder of this section will be to age-adjusted rates per 100,000.

Female Breast

The incidence rate for female breast cancer, which is shown in Table 3, rose significantly from 66.4 in 1960-1964 to 75.1 in 1965 ($p < .001$). The previous high for an annual rate was 70.0 in 1961. From 1962, when the incidence rate was 64.3, to 1965, the risk of breast cancer among women rose by 17%. Mortality due to breast cancer increased slightly from 27.3 in 1960-1964 to 27.5 in 1965.

Urinary

Cancer of the male urinary organs, primarily the kidney and the bladder, showed an increased rate of incidence from 1960-1964 to 1965. Most of the gain was in the rate for bladder cancer, which increased from 20.3 to 24.7, the highest annual incidence rate recorded for this site since the Tumor Registry began. The increase of 4.4 points was statistically significant ($p < .01$). The incidence rate of kidney cancer rose from 7.6 in 1960-1964 to 8.5 in 1965. Despite the increased incidence rates for males, there was a decrease in the mortality rate from all cancers of the urinary system among males from 10.8 in 1960-1964 to 9.0 in 1965.

The incidence rate of kidney cancer among women increased from 3.7 in 1960-1964 to 4.1 in 1965 and the rate for female bladder cancer rose from 6.2 to 6.9 in the same period. The mortality rate from urinary system cancer among females was nearly unchanged, increasing slightly from 4.0 in 1960-1964 to 4.1 in 1965.

Lung, Bronchus and Trachea

There was a rise in the incidence rate of cancer of the lung, bronchus and trachea among males from an average of 47.0 in 1960-1964 to 50.4 in 1965. There was also an increase in the rate for

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TABLE 1

PERCENT METHOD OF REPORTING CANCER CASES BY PRIMARY SITE AND SEX CONNECTICUT, 1965

		Total Cases				*Hospital Reported*		*Reported by Death Certificate Only*	
		Males		*Females*		*Males*	*Females*	*Males*	*Females*
ISC NO.	*Primary Site*	*No.*	*%*	*No.*	*%*	*%*	*%*	*%*	*%*
140-205	All Sites[1]	4,228	100.0	4,437	100.0	97.2	96.9	2.8	3.1
141	Tongue	44	100.0	15	100.0	100.0	100.0	—	—
143,144	Mouth	57	100.0	21	100.0	100.0	95.2	—	4.8
150	Esophagus	91	100.0	29	100.0	97.8	96.6	2.2	3.4
151	Stomach	237	100.0	142	100.0	95.8	91.5	4.2	8.5
153	Large Intestine	430	100.0	507	100.0	97.0	96.4	3.0	3.6
154	Rectum	267	100.0	201	100.0	98.1	95.5	1.9	4.5
155	Biliary Passages and Liver	65	100.0	71	100.0	86.2	93.0	13.8	7.0
157	Pancreas	129	100.0	85	100.0	94.6	90.6	5.4	9.4
161	Larynx	127	100.0	17	100.0	98.4	88.2	1.6	11.8
162	Lung, Bronchus and Trachea	718	100.0	155	100.0	96.8	94.2	3.2	5.8
170	Breast	8	100.0	1,207	100.0	100.0	98.1	—	1.9
171	Cervix Uteri	—	—	506	100.0	—	99.2	—	0.8
172	Corpus Uteri	—	—	275	100.0	—	99.6	—	0.4
175.0	Ovary	—	—	209	100.0	—	99.0	—	1.0
177	Prostate	564	100.0	—	—	97.5	—	2.5	—
180	Kidney	122	100.0	68	100.0	99.2	97.1	0.8	2.9
181.0	Bladder	357	100.0	124	100.0	98.9	98.4	1.1	1.6
190	Malignant Melanoma	52	100.0	59	100.0	100.0	98.3	—	1.7
193.0	Brain	81	100.0	72	100.0	98.8	93.1	1.2	6.9
194	Thyroid	19	100.0	45	100.0	100.0	97.8	—	2.2
197	Connective Tissue	39	100.0	30	100.0	100.0	100.0	—	—
200-202	Lymphatic Tissue	152	100.0	114	100.0	98.0	97.4	2.0	2.6
203	Multiple Myeloma	38	100.0	30	100.0	92.1	100.0	7.9	—
204	Leukemia	132	100.0	91	100.0	97.0	91.2	3.0	8.8
	All Other Sites	499	100.0	364	100.0	96.2	94.8	3.8	5.2

[1] Excludes non-melanotic cancers of the skin.

TABLE 2

CRUDE AND AGE-SPECIFIC INCIDENCE RATES OF CANCER BY SEX CONNECTICUT, 1965

	Males		*Females*	
Age Group	*No.*	*Rate Per 100,000*	*No.*	*Rate Per 100,000*
All Ages	4,228	305.4	4,437	308.0
0-34	151	19.2	311	39.6
35-44	197	106.7	500	262.3
45-54	523	302.0	820	462.2
55-64	1,001	810.5	916	683.6
65-74	1,338	1,724.2	1,000	1,051.5
75+	1,009	2,541.6	883	1,546.4
Age Unknown	9	—	7	—

females, from 7.4 in 1960-1964 to 9.4 in 1965, which was significant ($p < .03$). Mortality rates for cancer of the lung, bronchus and trachea did not show any appreciable changes from 1960-1964 to 1965: the rate for males decreased from 40.6 to 39.8 while the rate for females increased from 6.0 to 6.3.

Uterus

Cancer incidence rates of both the uterine cervix and uterine corpus increased from 1960-1964 to 1965 (from 31.9 to 36.8 and from 15.7 to 17.2, respectively). The former increase was statistically significant ($p < .005$). The main factor in the increased incidence rate for cervical cancer was a marked increase in the number of in situ cases, which comprised 64% of the total in 1965. The incidence rate of invasive tumors of the uterine cervix declined slightly from 1960-1964 to 1965. The mortality rate due to uterine cancer declined from 10.4 in the 1960-1964 period to 8.7 in 1965.

Stomach

Cancer of the stomach, which has long shown a downtrend in incidence, showed a further decrease in 1965 for both males and females compared to the 1960-1964 period. The incidence rate for males decreased from 19.0 in 1960-1964 to 16.3 in 1965 ($p < .05$) while the rate for females declined from 9.2 to 7.8 in the same interval. There were corresponding declines in the mortality rates: the rate

TABLE 3

AGE-ADJUSTED INCIDENCE RATES PER 100,000 IN 1965 AND 1960-64 BY SELECTED PRIMARY SITE AND SEX, CONNECTICUT

Primary Site	*Males* *1965*	*1960-1964*	*Net Change 1960-1964 to 1965*	*Females* *1965*	*1960-1964*	*Net Change 1960-1964 to 1965*
All Sites[1]	294.1	288.9	+5.2	273.4	262.7	+10.7
Tongue	3.0	4.0	—1.0	0.9	0.8	+ 0.1
Mouth	3.8	4.4	—0.6	1.2	1.3	— 0.1
Esophagus	6.3	6.5	—0.2	1.8	1.3	+ 0.5
Stomach	16.3	19.0	—2.7	7.8	9.2	— 1.4
Large Intestine	29.6	30.0	—0.4	28.6	29.5	— 0.9
Rectum	18.6	17.7	+0.9	11.8	11.9	— 0.1
Biliary Passages and Liver	4.5	5.0	—0.5	3.7	4.5	— 0.8
Pancreas	8.9	9.9	—1.0	4.6	5.9	— 1.3
Larynx	8.9	8.2	+0.7	1.1	0.8	+ 0.3
Lung, Bronchus and Trachea	50.4	47.0	+3.4	9.4	7.4	+ 2.0
Breast	0.6	0.8	—0.2	75.1	66.4	+ 8.7
Cervix Uteri	—	—	—	36.8	31.9	+ 4.9
Corpus Uteri	—	—	—	17.2	15.7	+ 1.5
Ovary	—	—	—	13.3	13.3	0.0
Prostate	38.5	38.7	—0.2	—	—	—
Kidney	8.5	7.6	+0.9	4.1	3.7	+ 0.4
Bladder	24.7	20.3	+4.4	6.9	6.2	+ 0.7
Malignant Melanoma	3.7	3.7	0.0	3.9	3.5	+ 0.4
Brain	5.7	5.3	+0.4	4.8	4.1	+ 0.7
Thyroid	1.4	1.0	+0.4	3.1	3.4	— 0.3
Connective Tissue	2.8	3.0	—0.2	1.9	2.3	— 0.4
Lymphatic Tissue	10.9	9.0	+1.9	7.1	6.1	+ 1.0
Multiple Myeloma	2.7	2.4	+0.3	1.7	2.0	— 0.3
Leukemia	9.1	10.8	—1.7	5.4	6.7	— 1.3

[1] Excludes non-melanotic cancers of the skin.

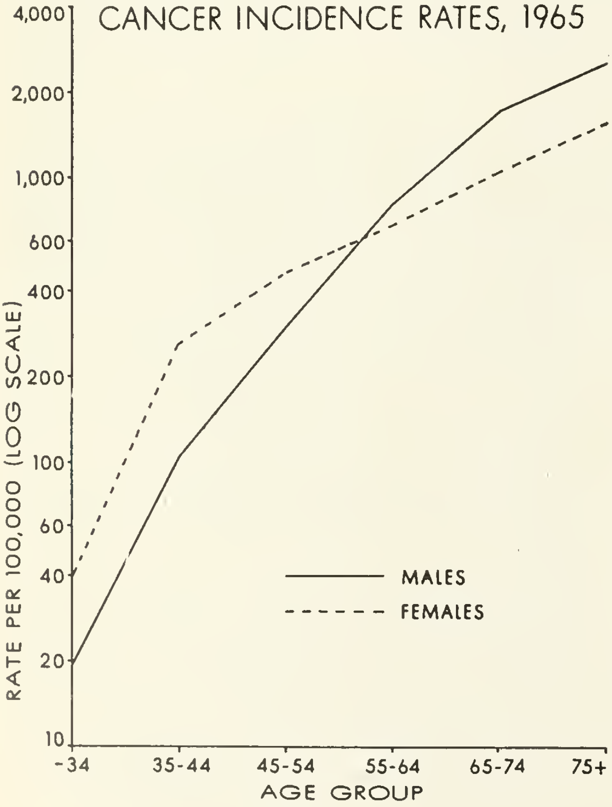

Figure 1

for males declined from 15.8 in 1960-1964 to 13.3 in 1965 while the female rate went from 7.6 to 6.3.

Age at Diagnosis

The risk of cancer in man generally rises as age increases. As shown in Table 2 and Figure 1, the risk of cancer in all sites in 1965 was about twice as great in women as in men, up to the age of 55. In the ages 55-64 the overall risk was about one-fifth greater for men while for the ages 65 and higher, the risk was approximately two-thirds greater for men.

The increased risk for women at the younger ages, compared to that for men, reflected primarily the incidence of breast and genital cancers, nearly half of which, among women, occurred under the age of 55. From age 65 on, the risk of prostate cancer among men increased rapidly and the incidence rates for cancer of the lung, bronchus and trachea and the urinary bladder among men exceeded the corresponding rates for women by substantial margins.

Treatment, Stage and Survival

Treatment

To be classified as first treatment, a procedure to remove, control, destroy or change tumor tissue, for

TABLE 4

PERCENT TREATMENT DISTRIBUTION OF CANCER CASES BY SELECTED PRIMARY SITE AND SEX[1]
CONNECTICUT, 1965

Primary Site, Sex	*Total Cases* No.	*Surgery Only* %	*Radiation Only* %	*Surgery Plus Radiation* %	*Chemotherapy*[2] %	*No Treatment* %
Stomach						
Male	227	43.2	1.3	—	6.6	48.9
Female	130	39.2	1.5	—	5.4	53.8
Large Intestine						
Male	417	76.7	0.5	—	2.0	20.9
Female	489	76.7	—	1.0	3.0	19.2
Rectum						
Male	262	70.2	3.1	2.3	2.6	21.8
Female	192	70.3	4.2	1.0	2.6	21.9
Lung, Bronchus and Trachea						
Male	695	19.7	21.6	6.3	11.3	41.0
Female	146	17.8	20.5	8.9	14.4	38.4
Breast						
Female	1,184	68.0	1.0	18.3	8.0	4.7
Cervix Uteri-Invasive	176	12.5	67.6	5.1	2.8	11.9
Corpus Uteri	274	41.2	20.1	32.9	2.1	3.6
Ovary	207	28.0	8.7	28.0	14.5	20.8
Prostate	550	27.3	1.1	—	47.1	24.5
Bladder						
Male	353	73.7	3.1	10.8	2.8	9.6
Female	122	64.8	6.6	9.8	3.2	15.6

[1] Based on hospital reported cases.

[2] Includes other therapy (surgery and/or radiation).

the purpose of either cure or palliation, must be initiated within 6 months of the date of diagnosis. The first-course treatment distributions for 10 major sites of cancer in 1965, based on hospital cases only, are presented in Table 4. Surgery alone was the treatment for 70% or more of the patients diagnosed with cancer of the large intestine and rectum, in 73.7% of the males with cancer of the urinary bladder and in 68.0% of the cases of female breast cancer. This was also the most frequent choice of treatment for patients with cancer of the stomach and uterine corpus.

Among invasive cancers only of the uterine cervix, two-thirds received radiation without other therapy. This finding is of interest in view of the fact that a 1966 study showed that better results were reported from surgery for localized cancer of the cervix than from radiation therapy.[5] About 1 patient in 5 with cancer of the lung, bronchus or trachea, or of the uterine corpus, received radiation alone as the first course of therapy. Surgery plus radiation was most frequently employed on a percentage basis for uterine corpus cancers (32.9%) and cancers of the ovary (28.0%).

Nearly half of the cases of prostatic cancer among males (47.1%) received chemotherapy, with or without other therapy in 1965. This mode of therapy was also used with 14.5% of the patients with cancer of the ovary and 11.2% of those with cancers of the lung, bronchus and trachea.

Stage

Stage of disease is based on all information available to the Registry as a result of physical examination, operative results, laboratory, X-ray and microscopic findings at the time of the first diagnosis of cancer.

The term "in situ" includes all neoplasms which are classified by the pathologist as being microscopically non-invasive. The term "localized" includes all neoplasms which are confined to the organ or site of origin. "Regional" includes all neoplasms with 1) extension to adjacent tissues not involving other organs 2) spread to regional lymph nodes or 3) both of these involvements. "Remote" includes tumors which 1) involve any other organ adjacent or distant 2) have metastasized to any distant part of the body or 3) are systemic in nature, such as leukemia.

The distributions of cases by stage of disease at diagnosis for 10 major sites are shown in Table 5. Notable was the high percentage of in situ cases

TABLE 5

PERCENT STAGE DISTRIBUTION OF CANCER CASES BY SELECTED PRIMARY SITE AND SEX[1]
CONNECTICUT, 1965

Primary Site, Sex	*Total Cases* No.	*In Situ* %	*Localized* %	*Regional* %	*Remote* %	*Unknown* %
Stomach						
Male	227	0.0	24.7	22.9	44.5	7.9
Female	130	0.8	30.0	22.3	36.2	10.8
Large Intestine						
Male	417	1.4	46.8	22.8	23.3	5.8
Female	489	0.6	46.4	22.5	21.9	8.6
Rectum						
Male	262	2.7	50.4	20.2	17.6	9.2
Female	192	2.1	47.4	19.3	23.9	7.3
Lung, Bronchus and Trachea						
Male	695	0.4	32.7	19.9	38.4	8.6
Female	146	—	28.1	20.5	45.9	5.5
Breast						
Female	1,184	0.9	50.2	38.0	8.4	2.4
Cervix Uteri	502	64.9	21.9	6.0	4.6	2.6
Corpus Uteri	274	6.6	76.6	7.3	8.4	1.1
Ovary	207	—	30.9	8.2	53.6	7.2
Prostate	550	0.2	60.4	6.9	18.9	13.6
Bladder						
Male	353	1.1	80.7	4.0	6.5	7.6
Female	122	—	73.8	4.1	12.3	9.8

[1] Based on hospital reported cases.

diagnosed among the cervical cancers (64.9%). The percentage of remote stage tumors was high for ovarian cancers (53.6%), cancers of the lung and related organs (males, 38.4%, females, 45.9%) and cancers of the stomach (males, 44.5%, females, 36.2%).

Survival

The relative survival rates at 5 and 7 years after diagnosis, for localized, regional and all stages of disease combined, are given in Table 6 for patients diagnosed in 1955-1959. The relative survival rate is the percentage that the observed survival rate is of the normal or expected survival for a similar group in the general population.

Among the 9 sites of cancer shown, the best results for all stages of disease combined at 5 years were obtained for women diagnosed with cancer of the corpus (71.5%) while the poorest results were those for males with cancer of the lung, bronchus and trachea (8.7%).

A female patient who was diagnosed with cancer of the ovary when localized had a 5-year relative survival probability of 65.3%, which was 2.5 times as great as the comparable rate for regional cases, 26.0%. At 7 years after diagnosis the survival probability for the localized ovarian cancer cases 2.8 times as great as the regional cases, 62.3% to 22.3%.

Among males diagnosed with cancer of the rectum in 1955-1959, the localized survival rate (63.6%) was 2.8 times as great as the regional rate (23.0%) after 5 years. After 7 years the localized rate (59.2%) was 3.5 times as great as the regional rate (16.8%). The highest ratio of localized to regional survival rate at 5 years was 5.1 for females with cancer of the lung, bronchus and trachea, based on relative rates of 30.3% and 6.0%.

Summary

An analysis of data from the Connecticut Tumor Registry shows there were increases in the age-adjusted incidence rates of cancer per 100,000 in 1965 for each sex, compared to the incidence rates during the 5-year period 1960-1964. The increase for females (from 262.7 to 273.4) was somewhat larger than that for males (from 288.9 to 294.1).

Two of the major increases in incidence rates by primary site occurred for female breast cancer (from 66.4 to 75.1) and male cancer of the urinary bladder (from 20.3 to 24.7). Other major changes in incidence rates from 1960-1964 to 1965 included increased rates of uterine cancer, lung, bronchial and tracheal cancer and decreases in the rates of

TABLE 6

RELATIVE SURVIVAL RATES (%) BY SELECTED PRIMARY SITE, STAGE AND SEX AT 5 AND 7 YEARS[1]
CONNECTICUT, 1955-59

	All Stages			*Localized*			*Regional*		
	No. of	*Surv. Rate*		*No. of*	*Surv. Rate*		*No. of*	*Surv. Rate*	
Primary Site, Sex	*Cases*	*5-Yr.*	*7-Yr.*	*Cases*	*5-Yr.*	*7-Yr.*	*Cases*	*5-Yr.*	*7-Yr.*
Stomach									
Male	988	12.1	11.2	209	34.4	32.0	278	8.9	7.5
Female	592	16.2	13.9	143	44.0	39.7	180	12.1	10.1
Large Intestine									
Male	1,584	41.0	38.3	704	67.8	63.8	377	30.4	28.3
Female	1,846	48.3	46.0	860	74.0	71.3	445	40.6	36.9
Rectum									
Male	1,072	37.8	34.2	510	63.6	59.2	204	23.0	16.8
Female	877	38.7	36.0	434	61.0	58.1	165	28.2	22.2
Lung, Bronchus and Trachea									
Male	2,067	8.7	7.0	449	23.1	19.3	536	9.4	8.6
Female	336	9.8	7.4	78	30.3	26.8	56	6.0	0.0
Breast									
Female	4,020	61.0	54.6	1,806	82.0	76.3	1,632	49.7	42.4
Corpus Uteri	1,267	71.5	69.6	915	83.2	81.6	95	39.9	39.5
Ovary	788	30.2	28.7	236	65.3	62.3	131	26.0	22.3
Prostate	1,826	49.6	40.1	960	64.1	55.5	93	42.8	34.7
Bladder									
Male	1,143	63.1	61.1	861	71.5	69.2	89	22.6	20.3
Female	370	69.1	68.1	275	81.5	81.4	31	24.7	22.9

[1] Based on hospital reported cases.

stomach cancer. Mortality rates for these sites in 1965 were mainly unchanged or lower compared to 1960-1964.

Surgery alone remained the primary form of treatment for cancer in 1965. A substantial proportion of the genital cancers and those of the lung, bronchus and trachea received radiation or chemotherapy, both with and without surgical treatment.

Two out of 3 cancers of the uterine cervix were diagnosed when not yet invasive. By comparison, about 4 out of 10 cancers of the stomach and the lung, bronchus and trachea were diagnosed at a remote stage of disease.

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The Fractured Jaw

A Medical-Dental Health Problem

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The mouth is the gateway to the digestive tract. It is also the source of human verbal communication as well as an important respiratory pathway. Any traumatic incident or surgical procedure which inhibits digestion, respiration, and communication represents a major insult to the health of a patient. The anatomic nature of jaw fractures and the techniques of treatment usually places them in the realm of dentistry, while interference with so many bodily functions represents a true medical problem.

It is the purpose of this paper to review recent experience with jaw fractures at Hartford Hospital in an attempt to illustrate the serious nature of these injuries and to demonstrate the need for both medical and dental concern for the well-being of orally-injured patients.

The hospital records of patients treated by the Oral Surgery Service for fractures of the mandible and maxilla from January 1967 to September 1969 were reviewed. The age of the patient, etiology of the fracture, treatment, length of hospitalization and complications were recorded.

Results

Analysis of 86 fractures of the upper and lower jaw reveal that it is a type of trauma most frequently found in males, in a wide age range (from 4 to 69 years). The mandible was more commonly affected than the maxilla (ratio of 6.5 to 1), but fracture of either bone was associated with other serious injuries in 31% of cases (table #1). Vehicular accidents and assaults accounted for 78% of these injuries (table #2).

Solitary fractures of jaws, when not associated with other injuries required only brief hospitalization, and the majority were treated by simple closed reduction (72%). Major complications were few (10%), but morbidity was high (table #3). Airway obstruction, dietary restrictions, and inhibition of speech are serious medical considerations in these patients.

TABLE 1

ASSOCIATED INJURIES

Cranial	10
Thoracic	2
Abdominal	2
Orthopedic	6
Multiple Injuries	7

Etiology: High speed vehicular travel and the human fist continue to be the major causes of jaw fracture. Other studies have noted that hospitals in high crime rate areas and those associated with frequent social disorders observe a high incidence of assault-type jaw fractures, whereas hospitals near highways or those in higher socio-economic areas record a higher incidence of automobile, sporting, and household accident type trauma.[1, 2] Facial impact against the automobile dashboard or windshield produces severe comminuted fractures of the mandible or mobilization of the maxilla, usually associated with oral-facial lacerations and loss of numerous teeth. All the patients in this series

TABLE 2

ETIOLOGY OF JAW FRACTURE

Motor Vehicular	38
Assault/fights	29
Falls	9
Bicycle	4
Sports	3
Gunshot	2
Pathological	1
	86*
Types of Fractures	
Mandible	71
Maxilla	11
Both	4

* Includes patients treated at Newington Veterans Hospital, Conn. Valley, and Mt. Sinai Hospital.

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TABLE 3
COMPLICATIONS

Airway Obstruction	preoperative 4 postoperative 1
Severe Hemmorrhage (blood replacement)	2
Osteomyelitis	1
Non-union	2

who were admitted to the hospital with serious cranial, thoraco-abdominal, or limb injuries, sustained their trauma in automobiles. While seat belts have reduced the overall incidence of serious injury due to vehicular accidents, the new cross-chest belts will, hopefully, prevent facial injury of the windshield-dashboard type.[3, 4] Fights, assaults, and sporting accidents account for the majority of simple fractures.

Bicycle accidents are the most common cause of childhood jaw fractures, most of which result from the child landing on his chin, causing condylar region fracture. Condyle fractures of the jaw in children, like epiphyseal fractures in long bones, may result in cessation of bone growth.[5] In this series, it is notable that three of the four children were riding the new "banana" type bicycles whose high seat and low curved handle-bars seem designed to propel the child forward onto his face.

Therapy: The basic surgical principles of the treatment of jaw fractures are similar to those of orthopedic surgery: reduction of the fracture, adequate stabilization, and prevention of infection. Re-establishment of the dental occlusion and preservation of teeth are, however, equally as important. Adherence to these principles is usually satisfied by closed reduction, accomplished by placing wires around the teeth and closing the mandible against the maxilla by wires or rubber bands. 71% of the fractures in this series were treated by closed reduction for five to six weeks. Open reduction was necessitated in 26% by gross displacement of fragments or inadequate teeth for dental wiring. Dentures, when intact or repairable, were often used as splints. Two fractures, which were undisplaced condylar fractures in adults, were not treated surgically, but were immobilized by chin supports.

The primary aim of the treatment of jaw fractures is re-establishment of the *functioning* dental occlusion. Whether treated by closed or open reduction, the teeth or dentures must be brought back into their pre-traumatic position. Failure to pay close attention to the position of teeth will result in permanent malocclusion and malfunctioning of the masticatory apparatus. All healthy teeth must be preserved to serve as the foundation for future reconstruction of the dental arch.

Fractured or infected teeth should be removed from the area of fracture, as prophylaxis against osteomyelitis. Staphyloccocal, streptococcal, and gram-negative organism can contaminate the fracture through oral wounds or infected teeth, resulting in deep bone infection, which in the jaws, is a painful, debilitating disease.[6] The one pathological fracture in this series was the result of osteomyelitis originating in an abscessed tooth.[7]

Four patients underwent tracheotomy. Bilateral mandibular fracture results in loss of control of the tongue, with posterior displacement into the pharynx, while oral hemorrhage can cause embarrassment of the airway. Two of these patients were comatose and the tracheotomies were performed for relief of airway obstruction, while the other two had profuse nasal and oral hemorrhage. Bleeding can usually be controlled by reduction of the fractures, but all oral wounds must be repaired prior to reduction. Only two patients required blood replacement as a result of blood loss from the oral cavity.

Complications: Airway obstruction must be prevented in all patients with jaw fractures. Emergency room therapy includes removal of bone fragments, teeth, dentures, saliva, and blood from the pharynx. A search should be made for missing teeth, fillings, or pieces of denture. Emergency room chest X-ray and examination of the pharynx may reveal these foreign bodies as the cause of respiratory embarrassment. In the obtunded patient, it may be necessary to retract the tongue forward by means of a lingual suture; while in the comatose state, tracheotomy should be given serious consideration.

In the post-operative period, airway complications may also be a serious problem. With the jaws wired into a closed position, vomiting can be life-threatening. One patient in this series vomited during the immediate post-operative period, becoming cyanotic and requiring *emergency* removal of wires. To prevent acute airway obstruction or aspiration pneumonitis, all medical and nursing personnel must be trained and alerted to remove the wires when necessary. Patients should carry a scissors at all times, to cut the wires, and they should be instructed in the use of antiemetic suppositories. Alcholic beverages should be forbidden.

While hospitalized, the patient must be carefully educated concerning his dietary needs and restrictions. While the average estimated weight loss in this group of patients was 15 pounds during the six week period of oral closure, some reported weight loss as high as 30 pounds! Carbohydrates and fats can be adequately ingested with a liquid diet of milk shakes and egg nogs, but protein deficiency and constipation are the major problems. Despite encouragement to use baby food and commercially available high-protein liquid dietary supplements, most patients soon grow weary of their use, and revert to soup and milk shakes. It is conceivable that a state of acute protein malnutrition or iron deficiency anemia could be reached in a six week period. Most of those patients with high weight loss complained of chronic fatigue and profound weakness by the end of this period. In such cases, periodic examinations by the patient's physician are warranted.

The most complex nutritional problem arises in the diabetic with jaw fracture. Frequent consultation among the dietician, physician and oral surgeon are mandatory to prevent a loss of medical control of the diabetes or the frequent occurrence of hypoglycemia.

The psychological and economic effects of jaw fracture are similar to those of other traumatic incidents or disease states which result in prolonged disability. Severe dietary restrictions, speech obstruction and chronic fatigue, however, often have the effect of producing a patient who is irritable, uncooperative, and unwilling to attempt even light work or return to school. Again, support from the physician can be an important factor in preventing severe depression, family chaos, or premature self-removal of fixation wires by the orally frustrated patient.

Conclusion

Jaw fracture is a serious injury which is potentially life-threatening and which leads to severe disability. Prevention of airway obstruction, malnutrition, and emotional depression, as well as treatment of the fracture, should be a concern of all medical personnel.

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APRIL 27, 28, 29, 1971

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Transposition Of The Great Arteries

Two Successful Open-Heart Corrections with the Mustard Operation

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N. S. Talner, M.D. and H. C. Stansel, Jr., M.D.

The *transpositions* are commonly encountered and are highly lethal anomalies of the arrangement of the great vessels. They are of various types, including those of *complete transposition of the great arteries* (with or without associated septal defects and valvular obstruction), incomplete transposition of the great arteries (Taussig-Bing and Double-outlet right ventricle), *corrected transposition of the great arteries* (with or without associated septal defects and valvular obstruction), *complete or incomplete transposition of the pulmonary veins* (total or partially anomalous pulmonary venous return), transposition of *the venae cavae,* and *dextrocardia.*[11]

Death early in infancy characterizes most of the transpositions without adequate associated defects. Early palliative or corrective surgery, especially with cardiopulmonary bypass has been recently utilized with increasing success.[2, 7] The most frequent form of the disease is complete transposition of the great arteries and we shall limit our paper to it, presenting the first two successfully operated cases in Connecticut and reviewing the literature with emphasis on the pathological anatomy and embryology, physiology, prognosis, available operations and their complications and results.

Case Reports

Patient R. C., #44-34-85

Admitted September 23, 1964, a nine-year-old white male, cyanotic at birth, who was catherterized and following the diagnosis of transposition of the great arteries, he underwent a Blalock-Hanlon operation at age 26 weeks. The patient did well until age 7, at which time he developed pneumonia and congestive heart failure requiring digitalization. Digitalis was stopped when arrhythmias developed and subsequently there was an interval of two years with relatively few symptoms. Recurrence of paroxysmal atrial tachycardia in 1964 prompted readmission, but cardiac catheterization was not repeated. On physical examination there was some cyanosis and clubbing as well as evidence of congestive heart failure manifested by rales, hepatomegaly and tachycardia, which soon became 230/min and required cardioversion, digitalis and quinidine for maintenance. *The patient had been recatheterized* at age five years and results shown in *Table 1* confirmed the presence of transposition of the great arteries with a large ASD, but without a VSD or pulmonary stenosis. Accordingly, he was accepted for operation and on *September 28, 1964,* a Mustard operation was performed. Following removal of the remaining atrial septum, a 2 x 4 inch pericardial patch was sutured in along the margins of the pulmonary veins so as to direct them to the right side. The patch was then continued as a running suture, interrupted about five or six places, and carried over so as to direct the caval blood back to the posterior ventricle and the pulmonary venous blood to the anterior ventricle. Following defibrillation, a normal sinus rate was present and after some support with vasoxyl, satisfactory cardiac action resumed. Postoperatively, the patient required diuretics, digitalization, and intensive pulmonary care, but definitely improved by the fifth day. A high nodal rhythm persisted but did not interfere with cardiac output and was usually above 75/min. On October 22, 1964, a venous angiogram was done and it showed contrast material entering an atrial chamber in a position which would be similar to the location of a normal left atrium. Contrast then passed to the left ventricle and out through the pulmonary artery. Pulmonary venous return was seen to be opacified and returned to an atrial chamber which occupied the right portion of the cardiac silhouette. Contrast material then passed to the right ventricle and out through the anteriorly placed aorta (Picture 1).

TABLE 1

PATIENT R. C. #44-34-85

O_2 Content *Vol. %*	*Pressure* *(mm Hg)*	
SVC	11.9	
RA	15	6
RV	15.4	120/8
LA	20.6	6
LV	18.6	45/9
PA	20.6	12 (mean)

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Picture I

Postoperative angiogram shows the contrast entering the SVC and then (through the patitioned atria); visualization of the LV and PA follow.

Subsequently, the patient was asymptomatic on digoxin except for a brief bout of serum hepatitis two and one-half months postoperatively. Six months postoperatively there was still a harsh systolic murmur but no thrill. Digoxin was continued and examination two years postoperatively showed the heart size diminished and the murmur decreased to grade II. Since then the patient has been off all medication and has enjoyed unrestricted activity. Recent examination five years postoperatively showed no clubbing, no cyanosis or cardiac murmur, but some residual cardiomegaly.

Patient M. L., #71-26-05

Six-year-old Greek girl born with cyanosis. There were frequent episodes of respiratory infections, exertional dyspnea and cyanosis even since she started walking. No fainting spells were noted, but growth was below the 3rd percentile for her age. P.H. and R.O.S. were non-contributory. On physical examination the patient appeared smaller than her age with bilateral arm BP of 100/70 and leg BP of 120/80. Significant oral and nailbed cyanosis were noted along with clubbing. The lungs were clear. There was no cardiomegaly or thrills. The S_1 was normal, but S_2 was single and accentuated. A grade 3/6 ejection systolic murmur was present along the LSB and was louder lower down, without radiation. The remainder of the examination was normal. The EKG showed right axis deviation with R.A. and R.V. enlargement, but there was greatly diminished P.A. segment with increase in the size of the descending aorta.

At angio the typical picture of transposition of the great arteries was seen and cardiac catheterization confirmed the presence of a large ASD with a systemic R. V. (R.V. pressure 115/5 mm Hg) and a pulmonary L.V. (L.V. pressure 60/9 mm Hg). Saturation in the L.V. was 88%, in the R.V. 65%, and in the aorta 72%. The hematocrit was 67%.

Accordingly, with the diagnosis of TGV and small PDA established, the patient was taken to the operating room on February 1, 1968, where it was proved that adequate perfusion was possible without ligation of the presumed ductus, dissection for which proved difficult and was abandoned. Under mild hypothermia at 32° F, the right atrium was opened widely following cannulation and after a piece of pericardium measuring approximately 2½" x 3½" had been obtained. A 1½ cm ASD was carefully enlarged and after visualization of the orifices of the pulmonary veins, the pericardium was sutured in place in the classical fashion of Mustard. This was performed without any difficulty. The right atrium was then closed and the caval slings removed. The heart was defibrillated with return of good cardiac action. Following replacement of additional 500 cc of blood, bypass was terminated and the wounds closed. The patient returned to the recovery room in good condition.

Postoperatively a bleeding diathesis was eventually controlled with fresh blood. The patient was extubated on the third postoperative day. She had been digitalized and diuretics were required along with fluid restriction in order to control a painfully enlarged liver on the fifth postoperative day. Subsequently she was discharged on the 22nd postoperative day.

Follow-up showed continuing improvement and both digoxin and diuretics were discontinued by the third month. She was acyanotic and 18-month follow-up by the referring physician showed her continuing her progress with cyanosis.

Discussion

A. *Pathological Anatomy and Embryology*

There are various associated anomalies in transposition of the great arteries. The main one, however, is a result of developmental failure in the embryo of 4 to 6 weeks. Instead of the normal *spiral* (225°) partitioning of the bulbus cordis with the resultant antero-posterior relation of the pulmonary artery to the aorta, there is a straight-line division (45°). Thus, the aorta ends anteriorly to the pulmonary artery and connects with the right ventricle. The pulmonary artery originates from the left ventricle and can be lying to the right, posteriorly or to the left of the aorta in the frontal plane.[3, 7, 11]

B. *Pathophysiology*

Anoxia from deficient oxygen supply to the periphery and to the myocardium itself results from inability to deliver pure pulmonary venous blood to the aorta. This is, of course, most severe if intracardiac shunting through associated atrial or ventricular septal defects is inadequate or even nonexistent. Because of the additional factor of frequently systemic pressure in both ventricular cavities and an increased cardiac output compensating for the maximal right-to-left and left-to-right shunts, congestive heart failure and generalized underdevelopment result.

Thus, cyanosis, attacks of hypoxia, pulmonary congestion symptoms and the signs of clubbing, as well as murmurs according to the associated defect present characterize the clinical presentation of these infants.

C. *Prognosis*

Prognosis of the untreated patient depends on the associated defects. Those who have none have the shortest life expectancy (0.11 years). In those where there is a VSD, but *also* increased pulmonary flow, the average expectancy is reported as 0.28 years. If, in addition to VSD, there is pulmonary hypertension, the average increased to two years, and if there is a VSD and pulmonary stenosis, it is 4.85 years. Finally, in single ventricle, the expectancy is 6.79 years.[2] As a group, patients with transposition of the great arteries have an *average* life expectancy of between one and three months since the most severe forms are the commonest. Occasional patients have lived to the second decade and, indeed, to the age of 36.[8]

D. *Palliative Operations*

Since the great majority of patients with transposition experience with hypoxemia or failure in the first few weeks of life, accurate and urgent diagnosis in this neonatal group is foremost. Although operations have been carried out elsewhere[7] without the benefit of cardiac catheterization and angiography, recent improvements in the intensive care of the newborn and the availability of image intensification fluoroscopy have made early diagnostic catheterization mandatory in our hospital.

(1) If the patient is found to be suffering from poor mixing at the atrial level, then a balloon atrial septostomy is carried out right there.[12] If this is unsuccessful and hypoxemia returns after two or three repeated attempts, then a sternotomy or thoracotomy is performed and an atrial septectomy is either carried out by a punch-type instrument or with the aid of a hook,[1] or by the method of Blalock and Hanlon or under direct vision with inflow occlusion and with or without pump oxygenator support or hyperbaric conditions. We prefer the open, inflow occlusion method. Transposition of the right pulmonary veins to the right atrium by redirection of the atrial septum or by Baffes operation,[4] (which also entails IVC to L.A. anastomosis) is a method that enjoyed some popularity in the past.

(2) If in addition to poor mixing or independently there is evidence of high pulmonary flow, then sternotomy and banding of the pulmonary artery is carried out with adjustment of the band so that the resulting distal pressure is approximately $\frac{1}{3}$ (one-third) systemic pressure. Balloon septectomy alone seems contraindicated in these patients since it would further increase pulmonary flow. In fact, the best results in the group have been obtained by the combined operation.

(3) If there is low pulmonary flow, then an end-to-side or side-to-side pulmonary artery to aorta shunt is carried out during the first six months of life. If the pulmonary stenosis interferes in later life, the Glenn operation (SVC to RPA anastomosis) may be preferable or even the Blalock-Taussig anastomosis. In the immediate newborn period, balloon atrial septostomy may be sufficient to increase flow to the lungs.

E. *Corrective Operations, Complications, and Results*

Early attempts to retranspose the major arteries were uniformly unsuccessful. Total redirection of atrial flow was the alternative and this was attempted with rare success by internal and external redirection of the orifices of the great veins and A-V valves through a variety of methods.[15] Finally, Senning[14] achieved a success with an intra-atrial patch and Bernard[5] reported a successful case with a tubular Teflon graft between the pulmonary veins and tricuspid valve. Consistently better results were not achieved, however, until the Mustard[10] operation was applied. In 118 patients[2] there were 45 deaths or an overall mortality rate of 30%. Individual series vary greatly in the mortality figures, however, and in 66 patients with transposition and intact ventricular septum, the mortality is 27% or 18 patients only. In selecting patients for total correction, attention must be paid to the following details:

1. *Preoperative evaluation*—Patients who have had an atrial septal defect-creating operation in infancy and no additional associated VSD or pulmonic stenosis constitute the best group for repair at any age after 2 to 3 years. Of course, the presence of fixed pulmonary hypertension would also severely compromise chances for survival, but this would be usually associated with a VSD.

Currently there have been some successful attempts to correct double outlet R.V. forms of TGV with VSD and P.S.[9] totally by a patch closure of the VSD and homograft bypass of the obstructed RV-PA outflow tract. This type of bypass obviates the need for sectioning major coronary arteries in attempting to resect the subpulmonic stenosis.

Rastelli[18] used an internal shunt through the VSD from the L.V. to the aorta, with homograft reconstruction of the RV-PA continuity.

2. *Operative Considerations*—An adequately sized pericardial patch must be used. This for all practical purposes means almost the entire available pericardium between the two phrenic nerves laterally, the great arteries' pericardial reflection above and the diaphragmatic surface below.

The suturing should consist of anchoring sutures with continuous technique in between. If the patch appears very redundant at the end, it can be plicated or part of it can be excised and in turn used to enlarge the right atrium Diagram I).

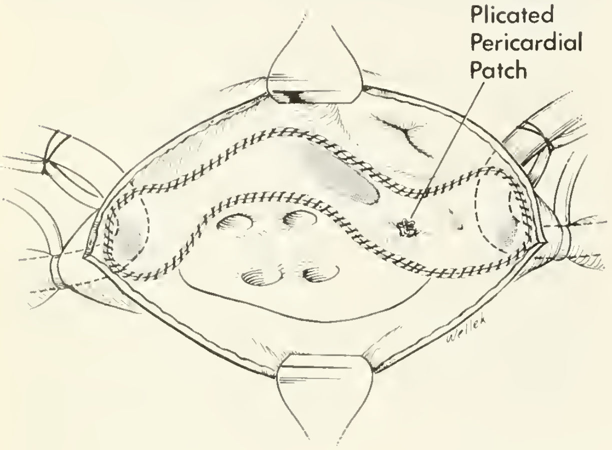

Diagram I

The venous cannulae should be out of the way of the repair and inserted very close to the orifices of the SVC and IVC so that they can be easily excluded from the pulmonary ventricuspid valve chamber when the baffle is inserted and they are viewed from within (Diagram II).

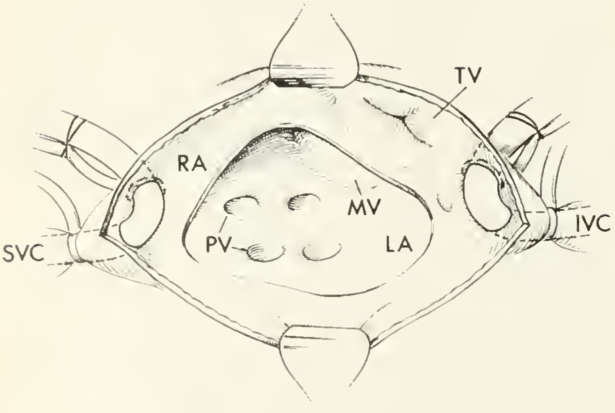

Diagram II

Care must be taken to avoid heart block when suturing between the atrial septal ridge and tricuspid valve. The coronary sinus may be allowed to drain into the tricuspid valve. Hemostasis must be thorough, especially since pulmonary edema has been described with a mediastinal hematoma compressing the right atrium, which, in turn, compressed the baffle and obstructed the pulmonary venous flow to the tricuspid valve. Successful operative relief by evacuation of clots has been reported.[6]

3. *Postoperative care*—Frequent respiratory difficulties make the use of continuous positive pressure respiration with an endotracheal tube mandatory in most patients. A tracheostomy can usually be avoided. Some degree of central venous pressure elevation is preferred in order to keep the newly transposed atrial conduits capacious. Digitalization is continued or started only with specific indications. Diuretics are usually necessary, although for a temporary period only.

Summary

The first two successful surgical corrections of transposition in Connecticut are reported. A review of the pathological anatomy and physiology along with a discussion of indications for palliative and corrective surgery follow. Points about the management of these patients are stressed in the preoperative, the operative, and the recovery periods.

Addendum

Since the writing of this paper, an additional three patients have been operated at Yale-New Haven Hospital. All five patients are doing well.

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MY FATHER WAS A COUNTRY DOCTOR

One day this old-fashioned country doctor was called to the home of some city people who came there for the summer. Their little girl had fallen out of a tree and broken or fractured her wrist. My father looked at it all over. He went out with his jackknife and cut off a little crotched forked stick from a little bush or tree that was growing there. He came back and fitted this thing to the broken joint, bound it with a bandage and plaster. Well, quite understandably, the people felt perhaps that this was a rather crude performance. They summoned, as they were able to do, the best surgeons and experts from New York City. When two of these really wise and expert men came up the river, they looked at the bandage and asked where it came from. When they were told the simple little story, they shook their heads and smiled. They said, "With all our equipment, with all our laboratories, and with all our investigation centers and with all the things we have, we couldn't have produced anything that is so exactly what is needed as that little forked stick cut off a bush by the roadside."—Sherrill, Rt. Rev. Henry Knox: Edwin Jan van Etten, *Cathedral Sermons* (*Boston*) Oct. 20, 1963.

THE PRESIDENT'S PAGE

The recent Annual Convention of the AMA was different from those of the past two years in that the business of the House of Delegates was not disrupted by representatives of dissident groups. This was due in part to the tight security provided. However, the Consumer's Forum conducted by Reference Committee J also was a factor. The five man Committee was augmented by four members of the AMA Board of Trustees and the AMA Vice President, Dr. Louise Gloeckner. Immediately following the opening statement of the Committee Chairman, Dr. Malcolm Todd of California, the consumers took charge of the meeting and elected their own chairman. Dr. Todd stood his ground and eventually the two chairmen cooperated with one another so that a fairly orderly hearing was held. Time did not permit all those wanting to speak to be heard. However, the representatives of the minority and disadvantaged groups were given ample time to voice their criticisms and offer suggestions. Among these were more personal attention and greater compassion, both of which I mentioned in my last month's President's Page as criteria for measuring the quality of medical care. Also suggested was the creation of a multi-ethnic council to advise the medical profession, greater enrollment of minority and disadvantaged students in medical schools and allied health training programs, expansion of mechanisms by state and local medical societies to provide dialogue with health care consumers, and increased support by the AMA of health care in disadvantaged areas with emphasis on preventive medicine and correction of the maldistribution of health care personnel.

On the subject of abortion divergent views were expressed. The chant of "free abortion on demand" was heard from many young women. A man who opposed abortion and stated that liberal abortion practices were advocated by the Marquis deSade (from whose name sadism is derived) had to retreat from the podium to avoid physical harm from the aroused women.

The reference Committee recommendations included consideration by the AMA Board of Trustees of 1) the creation of a multi-ethnic advisory committee on health care problems of minority groups and 2) establishment of a reference committee to hear the views of consumer and other public groups concerned with health care at each Annual and Clinical Convention of the AMA. I hope the trustees will respond favorably to these suggestions. It is important that there be dialogue with health care consumers at all levels of organized medicine—national, state, county and local. The understanding of one another's problems and goals that this produces will be helpful to both.

The shortage of medical manpower is serious and will probably become more serious in the near future. In an effort to combat this, the increased use of allied health personnel is being recommended. In Colorado they are training Pediatric Nurse Practitioners and in Illinois they are training Nurse Midwives. The newly-installed President of the AMA, Dr. Walter C. Bornemeier, in his inaugural address, offered a five-point program directed toward this problem. This included shortening the medical school curriculum, modernizing and shortening residency programs, relating more of the training of students to patient care at an earlier point, assimilating many full-time professional teachers into patient care and reducing the number of medical research institutions and researchers. He estimated that this would provide 50,000 physicians for patient care. In discussing the length of the residency programs he contended that the resident in his later years was getting less training and providing more service. This was a benefit for the attending physician. He also estimated that $5.00 of the daily hospital charge was for the hospital's residency or educational program. He suggested that the Pre-med—Medical School curriculum could be shortened to 6 years, and that the pre-clinical subjects be taught in the University, thus avoiding duplication of laboratory facilities and teaching staff in both the University and the Medical School. This is similar to the suggestion offered sometime ago by the Dean of the Harvard Medical School that the medical schools be closed and the pre-clinical subjects be taught in the University and the clinical work in the Community Teaching Hospitals.

Dr. Bornemeier's ideas are very challenging and warrant serious consideration. He has requested the AMA Board of Trustees to make an "in depth" study of current residency programs. However, this still does not answer the problem of maldistribution of physicians or the lack of primary physicians (general or family practitioners, internists, and pediatricians). Statistics show that general or family practitioners are decreasing in number per 100,000 population and internists and pediatricians are increasing. However, the increase is not enough to offset the decrease so that the combined total is less now than 10 or 20 years ago. New methods must still be devised to correct the maldistribution of physicians and to provide more primary physicians.

MORRIS A. GRANOFF, M.D.

I have steadily endeavored to keep my mind free so as to give up any hypothesis however beloved (and I cannot resist forming one on every subject) as soon as facts are seen to be opposed to it. Indeed I have had no choice but to act in this manner for with the exception of the Coral Reefs, I cannot remember a single first-formed hypothesis which had not after a time to be given up or greatly modified. . . . This has naturally led me to distrust greatly deductive reasoning in the mixed sciences.—*Charles Darwin*

Anesthesiology Grand Rounds
Yale-New Haven Hospital

Bilateral Abductor Paralysis

Samuel M. Lerner, M.D., John A. Kirchner, M.D. and Frederick W. Hehre, M.D.

Dr. Samuel M. Lerner:

A 52 year old female was admitted to Yale-New Haven Hospital for thyroidectomy. She complained of increasing hoarseness and difficulty in swallowing during the previous 10 months.

Past history revealed D&C's for incomplete abortion in 1948 and 1956, and cauterization of the cervix for chronic cervicitis in 1965. Physical examination revealed an enlarged, hard, nodular thyroid gland. Fluoroscopy showed extrinsic pressure on the lateral aspect of the esophagus at the thoracic inlet. Laboratory data were within normal limits. Since she had received halothane in the past, nitrous oxide was chosen as the primary anesthetic agent.

The patient was premedicated with pentobarbital 150 mg, hydroxyzine 100 mg; and atropine 0.5 mg. Anesthesia was induced with intravenous thiopental 250 mg. and maintained with nitrous oxide and oxygen at a flow rate of 5 liters to 2 liters. Succinylcholine 50 mg. was used to facilitate endotracheal intubation. Curare 15 mg. was given to prevent coughing and straining during operative tracheal manipulation.

At operation, the thyroid gland was hard, fibrous and adherant to the trachea. Frozen section revealed Hashimoto's Struma and total thyroidectomy was performed. After one hour and 20 minutes of anesthesia, 1 mg. of atropine and 2.5 mg. of prostigmine reversed the effect of the curare and the patient was extubated. The vocal cords appeared to move when examined by direct laryngoscopy.

The patient was admitted to the recovery room awake with slight inspiratory stridor. Her respiratory distress increased in severity and necessitated reintubation. Hydrocortisone 200 mg. and high humidity were administered to ease her breathing. She showed no evidence of residual curarization. Three hours later, the patient was extubated again, but pronounced inspiratory and expiratory stridor and severe respiratory distress were present and the endotracheal tube was again reinserted. At this time the vocal cords showed no movement. The patient spent the night in the Intensive Care Unit in a high humidity oxygen tent with an endotracheal tube in place.

The following morning the patient was again extubated but she breathed adequately for only two hours. Respiratory distress necessitated reintubation, and following that a tracheotomy was performed.

Dr. Nicholas M. Greene: How soon after the patient was extubated postoperatively was the reintubation necessary?

Dr. Lerner: About 10 minutes.

Dr. Greene: Why was high humidity oxygen given through the endotracheal tube?

Dr. Lerner: It was thought that the respiratory obstruction might be due to edema of the vocal cords and with steroids and high humidity the edema would subside.

Dr. Greene: Wouldn't the high humidity go right past the cords?

Dr. John A. Kirchner: I am interested in the movement seen in the vocal cords immediately after extubation. Did the cords abduct even one time? This is critical. Was there just fluttering movement?

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DR. FREDERICK W. HEHRE, is Attending Anesthesiologist and Associate Director, Yale-New Haven Hospital, New Haven, Connecticut.

From the Division of Anesthesiology and the Section of Otolaryngology, Yale University School of Medicine and the Departments of Anesthesiology and Otolaryngology Yale-New Haven Hospital.

Dr. Lerner: Yes, only a fluttering movement with tendency toward adduction, especially on inspiration. There was no active abduction. It was difficult for an inexperienced laryngoscopist to make that judgement.

Dr. Kirchner:

It is difficult even for an experienced laryngoscopist. Both recurrent laryngeal nerves in an animal can be cut and it is very difficult by inspection to say that both recurrent nerves had been cut. Cut one nerve, and, under anesthesia, it is difficult to tell which nerve on which side had been cut. Other things influence the motion of the vocal cords; the passage of air and the activity of the crico-thyroid muscle. The recurrent laryngeal nerve supplies all the laryngeal muscles except the crico-thyroid muscle, which is supplied by the superior laryngeal nerve. The crico-thyroid is the strongest adductor of the vocal cords. It rocks the cricoid forward on the thyroid cartilage pulling the cords together, stretching and adducting them. When the recurrent nerve is cut the cord assumes a paramedian position, but not as tight as if this nerve were intact. Practically, it is in the midline. If both cords are in the midline, the patient will be able to phonate and speak in a normal voice. This woman can speak normally, but when she stops to breathe, she has stridor. This is not true if the vagus nerve is injured at the ganglion nodosum, because the superior laryngeal nerve is also damaged, and the crico-thyroid does not function. The picture seen is complete paralysis of all the muscles of the larynx resembling that when a muscle relaxant is given prior to intubation. The cords are in intermediate position, apart, but not completely apart. The intermediate position allows a good airway but no voice. In vagus injury near the base of the skull, the cords never come to the midline and the patient has a breathy voice but a good airway.

Normally in inspiration the cords abduct and on phonation they adduct. Bringing the cords to the midline is a function of the crico-thyroid muscle. The crico-thyroid gives gross adduction and the vocalis provides fine adjustment for singing or for certain types of voice production. If one recurrent nerve is cut, the glottis looks normal on phonation. When the patient with unilateral recurrent nerve injury tries to inspire, the involved cord does not move away from the midline while the normal one does, and the patient has no dyspnea because only half the glottic chink is needed at rest. If this patient climbed stairs or engaged in strenuous physical activity, the cord acts as a hammock-shaped valve, traps the incoming stream of air and flutters. Some patients with unilateral vocal cord paralysis have a normal voice but if they get a crumb caught in their throat and have to cough or move air quickly, they get stridor, because of the upward slope of the cord and the Bernoulli effect. The larynx is a tube narrowed at the vocal cords, where the pressure is decreased and the air passes faster so the cords are sucked together. Stridor under ordinary conditions is caused by the Bernoulli effect and the shape of the free edges of the cords.

When the crico-thyroid muscle contracts, it rocks the cricoid back, carrying with it the arytenoid cartilage, stretches the cord and brings it to the midline. This is the muscle that causes the respiratory obstruction. One treatment for this is to cut one or both superior laryngeal nerves, which supplies motor fibers to the crico-thyroid muscle. The posterior crico-arytenoid muscle is apparently driven by the respiratory center. When the recurrent nerve is cut, this muscle no longer functions.

What causes nerve injuries at thyroidectomy? First, the recurrent nerve may branch outside the larynx. Anatomic dissection reports state that 30% to 90% of patients have branches outside the larynx. Some branches are sensory from the trachea and the esophagus and not motor branches. This can be very confusing when a surgeon finds such a branch. He assumes this branch to be the recurrent nerve and carefully preserves it. Then in taking out the gland, he removes the nerve trunk with the gland. Armstrong and Hinton found as many as 5 branches outside the parynx in 1% of their subjects, 4 branches in 7%, 3 branches in 26%. Secondly, the nerve may be damaged because of its variable relation to the inferior thyroid artery so when the gland is retracted, the nerve may be pulled up and cut. The relationship to the artery cannot be depended upon. Also, on the right side, the recurrent nerve may occasionally simply loop and enter the gland without descending around the subclavian artery. Thirdly, the nerve can be crushed in the clamp during attempts at hemostasis; or caught in a tie. It can be stretched and divided during dissection. Involvement in scar tissue is hypothetical and probably not as important.

Discussion

Dr. Greene: What should we look for when we are asked to laryngoscope a patient at the conclusion of a thyroidectomy following extubation?

Dr. Kirchner: When a tube has been in place for several hours, the soft tissues will have been pushed apart and will stay there for a while. This may account for the error that motion that was present. I doubt that there was real motion in this case. It must have been passive; that is, disturbance by the passage of air or by the crico-thyroid muscle stretching the cord. You must look for active abduction of the cords. If the cord is near the midline and actually moves laterally, particularly rhythmicly several times, the nerves are intact and the prognosis is good. We wait 6 months before recommending permanent surgical correction because a nerve that has been crushed, tied or stretched may recover function up to 6 months. After 6 months I know of no one who has observed function or return of a paralyzed cord.

Dr. Peter Chodoff: Then she has bilateral abductor paralysis?

Dr. Kirchner: Yes. Unilateral paralysis frequently goes unrecognized because otherwise she would not have stridor and would have a normal voice. A large Swedish series, which examined every patient after surgery, even asymptomatic ones, showed a significant number with unsuspected unilateral recurrent nerve paralysis.

Dr. James I. Gilman: Could her thyroid disease involve the recurrent nerves?

Dr. Kirchner: The vocal cords should be examined before thyroidectomy. With thyroid malignancy, one cord may be paralyzed before operation, but, if both were paralyzed, there would be symptoms.

Dr. Romulo L. Villar: It has been reported that following manipulation of the recurrent nerve, the abductors are more vulnerable to injury.

Dr. Kirchner: We don't agree. Semon's idea that the abductors are more vulnerable than the adductors has been discredited. That theory is explainable on there being one more adductor (the cricothyroid) than abductor.

Dr. Greene: Would you suggest that patients should be laryngoscoped at the conclusion of operation under light or no anesthesia or under moderately deep anestheisa? If they are very light, they might go into laryngospasm and one would not be able to see abduction.

Dr. Kirchner: Unless the patient went into real laryngospasm, I think that they occasionally gasp. If you see one abductor cycle, you are in business.

Dr. Greene: Is it worthwhile putting any reliance on laryngoscopy at the conclusion of thyroidectomy?

Dr. Kirchner: There is little to be learned unless the patient is light. It is really meaningless if a tube has been in for a while.

Dr. Greene: What has been the subsequent course of this patient?

Dr. Kirchner: After 4 months, she continues to have motionless midline vocal cords, and is wearing a tracheotomy cannula. If by the 1st week of June if she cannot breathe without her cannula, or, if she still has motionless vocal cords, we will admit her for a unilateral arytenoidectomy.

Dr. Greene: Can she phonate by closing off the cannula?

Dr. Kirchner: Yes. She has a fairly good voice.

Dr. Luke M. Kitahata: If the recurrent nerve is stimulated what happens to the abductor and adductor muscles?

Dr. Kirchner: It depends on the frequency of stimulation. At less than 30 cycles per second, there will be a series of abductions of the cords. Over 30 cycles per second there is increasing adduction. Retching and gagging can also produce increase in pressure. There are afferent nerves in the recurrent nerve as well as motor nerves and no one can quite sort out the true cord movements from the retching and gagging.

Dr. Gilman: Has anyone anastomosed cut nerves?

Dr. Kirchner: Yes. There are reports in which the recurrent nerve has been found and anastomosed very carefully. The poorest way of assessing vocal cord function is visual observation because of artifacts with air movement and gagging. No one who has re-anastomosed the recurrent nerve has ever observed abduction of the cord.

Dr. Etsuro Motoyama: What happens to the vocal cords during exhalation? Do they narrow?

Dr. Kirchner: It depends partly on the depth of anesthesia. It narrows but this is a passive movement. My associate, Dr. Murakami, working with animals at various depths of anesthesia, levels of CO_2 and oxygen, has observed that the only active muscle in quiet respiration is the abductor muscle, the posterior crico-arytenoid. Movement back towards the midline is passive.

LAW—MEDICINE NOTES

J. Alfred Fabro, M.D.

Strunk v. Strunk

This case involved the request of the mother of a mentally incompetent ward of the state to permit removal of one of his kidneys for transplantation into his brother who was being kept alive with frequent dialysis, which it was considered could not be continued much longer. This was the first such case to come before the highest court of any state in this nation or the federal courts.

The courts held, in a 4 to 3 decision, that it did have the right to make such a decision, and gave such permission.

Tommy Strunk was 28 years old, married, employed, and a part-time student at a university. He was suffering from chronic gomerular nephritis. Jerry Strunk, his brother, was 27, mentally incompetent, in a state institution for the feeble-minded, with an IQ of 35 corresponding with a mental age of about 6 years.

It had been determined that Tommy would need a kidney to survive. His mother, father and collateral relatives had been tested, but were not medically compatible as live donors. Jerry was, however. So the mother petitioned the court for authority to proceed with the operation. When an individual is a minor, or mentally incompetent, or unable to give consent, the nearest of kin or guardian can legally give consent—if the procedure or operation is for his benefit. Removing a kidney, without more, was of course of no benefit to Jerry.

Testimony, including that a psychiatrist, established that Jerry was very close and dependent on his brother. He was the only person to whom he had any attachment. It was his opinion that the death of Tommy under these circumstances, would have "an extremely traumatic effect on him."

The Department of Mental Health testified that though Jerry was a mental defective, his emotions and reactions were on a scale comparable to a normal person. Balancing the seriousness of the operation to Jerry and the traumatic effects on him of the loss of his brother, it believed that the donation of a kidney was justified.

As to the effects of the loss of a kidney, it was admitted that the long term risk is increased in living donors, estimated at 0.07 per cent by Hamburger. The risk was compared to that incurred by driving a car for 16 miles every working day (Merrill, 1964).

The court held that weighing all the advantages and disadvantages of donation of a kidney by Jerry to his brother, the operation was justified.

Speaking for 3 judges, the dissent stated: "My sympathies and emotions are torn between a compassion to aid an ailing young man and a duty to fully protect unfortunate members of society."

The dissent did not agree that loss of a close relative or friend to a mentally 6 year old child was of a major psychological impact. "Furthermore, there are no guarantees that the transplant will become a surgical success. . . . The life of the incompetent is not in danger, but the surgical procedure advocated creates some peril."

He concluded: "To hold that committees, guardians, or courts have such awesome power even in the persuasive case before us, could establish legal precedent, the dire result of which we cannot fathom. Regretfully I must say no."

Strunk v. Strunk, Court of Appeals of Ky., 1969.

Doctor's Office

Michael P. Atkins, M.D. and Charles G. O'Connell, M.D. announce the opening of their office for the practice of obstetrics and gynecology, Main Street, Somers, Connecticut.

Joseph F. J. Curi announces the opening of his office for the general care of infants, children and teenagers, Litchfield Hills Medical Center, Torrington, Connecticut.

Stephen Lirot, M.D. announces the reopening of his office for the treatment of diseases of the eye, ear, nose and throat, 53½ West Main Street, Meriden, Connecticut.

Carlton R. Palm, M.D. announces the opening of his office for the practice of pediatric allergy, 123 York Street, New Haven, Connecticut.

DR. J. ALFRED FABRO, Senior Attending Surgical Staff of the Charlotte Hungerford Hospital, Torrington, Conn.

Electrocardiogram of the Month

Yale-New Haven Hospital
New Haven, Connecticut

Prepared by
HYMAN M. CHERNOFF, M.D.
Associate Professor of Clinical Medicine,
Yale School of Medicine
Director, Dept. of Electrocardiography
Memorial Unit, Yale-New Haven Hospital

Tall upright T-waves may occur in the chest leads in a variety of clinical states, both normal and abnormal. Below are examples of such tall T-waves obtained from a number of different patients. Although the tall T-waves in each case tend to resemble one another, there are slight differences that may help point to the etiologic factor in each case.

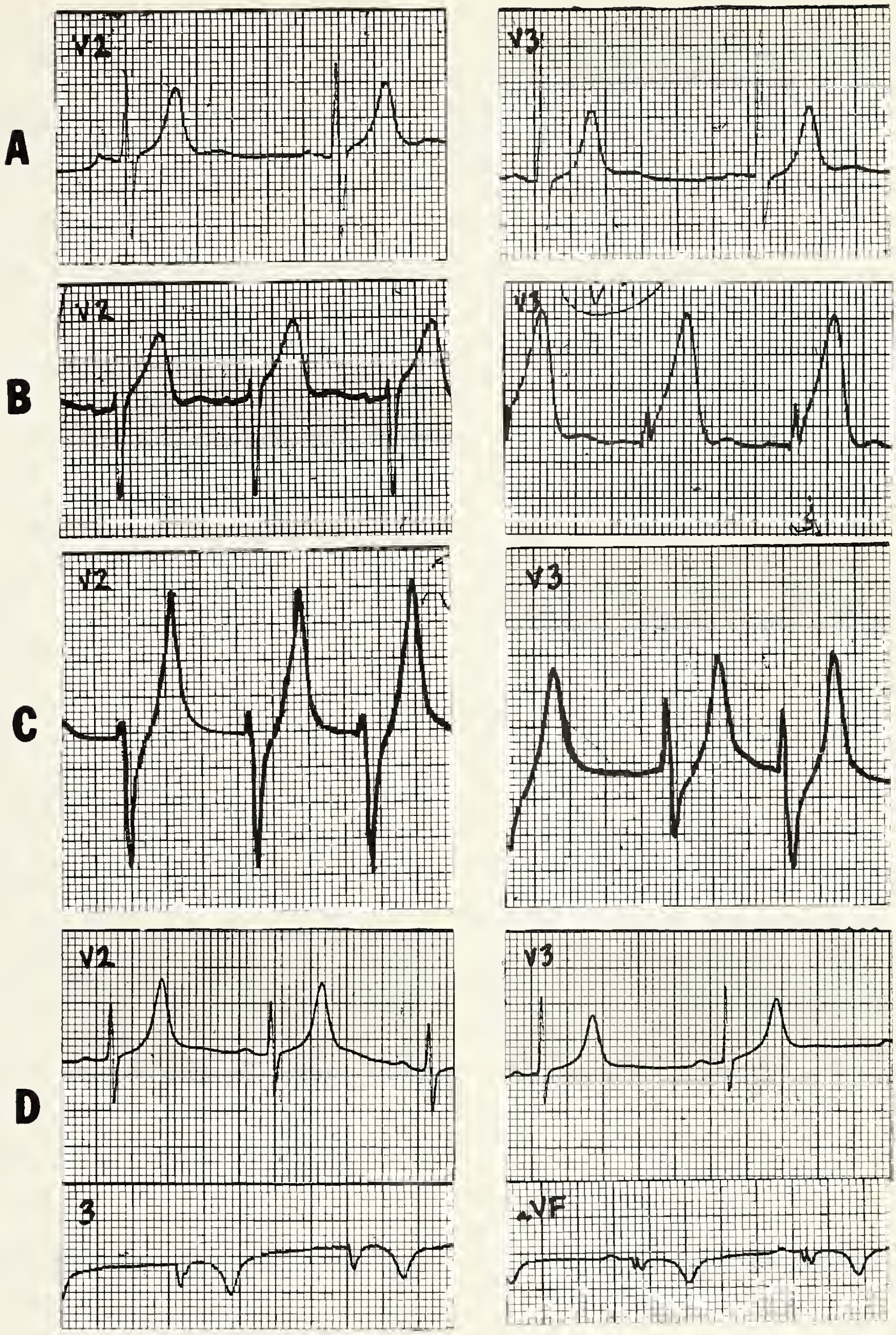
FIGURE A exhibits leads V2 and V3 in a normal young athlete with sinus bradycardia. In the presence of bradycardia the T-waves in the chest leads may be quite tall. Such tall T-waves tend to exhibit asymmetrical limbs with the upstroke of the T-wave slower than the downstroke. A prominent U-wave usually follows such tall T-waves, and the K-QT value is within normal limits.

FIGURE B exhibits leads V2 and V3 in a patient who was experiencing severe substernal chest pain of several minutes duration and in whom subsequent serial electrocardiograms revealed classic patterns of recent infarction of the anterior septal area. In the early stages following occlusion of the anterior descending branch of the left coronary artery the T-waves in some of the chest leads may become quite tall (so-called hyperacute T-waves). This may be the only electrocardiographic abnormality noted on admission to the hospital. These T-waves tend to be asymmetrical. U-waves may follow these T-waves.

FIGURE C exhibits leads V2 and V3 in a patient with chronic renal disease in whom the serum potassium became elevated to 8.2 m.Eq. per liter. When hyperkalemia is the cause of tall T-waves, the T-waves tend to exhibit symmetrical limbs (so-called peaked or tented T-waves). The U-wave becomes minute or disappears altogether. The K-QT value may shorten.

FIGURE D exhibits leads V2, V3, and leads 3 and aVF in a patient who had recovered from a postero-inferior wall infarction. The tall T-waves in V2 and V3 tend to have symmetrical limbs and are the mirror image of the symmetrically inverted T-waves that are usually seen in the evolved pattern of an anterior wall infarction. When posterior wall infarction is the cause of tall symmetrical T-waves in the chest leads, the R/S ratio in the right-sided chest leads becomes greater than 1.

Tall upright T-waves have also been noted in the chest leads on occasion in patients with alcoholic cardiomyopathy and also in patients with a variety of intra-cranial disorders such as neoplasm, cerebral accidents, drug-induced coma, myxedema coma, cerebral trauma, etc. In such cases the QT intervals usually are prolonged and the U-waves prominent. The cause of these changes is not known.


A
V2
V3
B
V2
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C
V2
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D
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Letter To The Editor

Members of the Society are invited to communicate with the Editor expressing their opinions or giving information as to any matter of interest to the members. The Editorial Board reserves to itself the right to select the communications or excerpts therefrom that will be published and to reject others. As with other material which is submitted for publication, all letters will be subject to the usual editing. Address all correspondence to: THE EDITOR, CONNECTICUT MEDICINE, 160 St. Ronan Street, New Haven, Connecticut 06511.

To the Editor:

Treating Narcotic Addicts

Marathon House (Mass.) Medical Director Judith Eden, M.D., told the June meeting of the New London County Medical Society about a realistic approach to narcotic addiction. After describing the addict's personality and contributing factors she outlined the Marathon program: rationale, modus operandi and results.

The personality of the addict is a mixture of protracted adolescent instability and sociopathy. He (or she) is immature and dependent, avoiding responsibility and growing up, searching for the easy way, and preferring drugs to coping. The addict must have drugs to maintain his image (Marlon Brando) and he protects it with rationalizations, e.g., the whole trouble is his spouse, the ghetto, or Vietnam.

Under the addict's facade is inadequacy and a poor self-concept. He has trouble feeling good about himself—as a person, as a man.

What are the factors leading to and sustaining addiction? Publicity, glamor and use by models (Timothy O'Leary) are among them. And there is The Pill Society, sustained in part by some physicians.

A diagnosis of drug dependency must be considered when a young person's behavior shows a drastic change, e.g., more than the usual withdrawal or rebelliousness. Another indication is disappearance of household objects such as T.V. sets.

Turning to treatment Dr. Eden said that the psychotherapies are ineffective. Addicts are only too happy to spend time in individual or group therapy, talking about the past instead of the here-and-now and dealing with it. (She noted that methadone treatment usually allowed addicts to skip the main point—the personality—and the person remained drug dependent.)

Marathon House type programs are run exclusively or primarily by addicts and ex-addicts. The method: peer group pressure for self-help and growing-up. Groups are the major tool. In them addicts talk about, and face, feelings—fear, self-doubt, wanting one's own way, wanting to run away—*real* feelings with "the music matching the words."

Consequences of behavior are stressed. Eighty-five percent of "brothers" and "sisters" have been in jail. Says Dr. Eden,

"We don't take volunteers because they don't stay. Jail makes (addicts) face consequences."

Last fall Marathon House, in operation two years, produced 16 "graduates." Follow-up has been easy because graduates remain "closely connected" and "brothers" and "sisters" readily find out what they are doing. Graduates who feel they are slipping come back briefly "to experience some real concern."

So far four of five graduates have cut the Marathon House apron strings. Living independently, they still 'phone, keeping in touch with the program that gave them a new way of life.

Note: Although "the answer" to treatment of narcotic addiction has yet to be found, Marathon House is a model, shaping programs such as that at Connecticut's Valiance House at Norwich Hospital.

Morgan Martin, M.D.
Superintendent, Norwich Hospital

Norwich, Conn. 06360

The Connecticut State Medical Society offers placement assistance through the Physicians Placement Service, 160 St. Ronan Street, New Haven, Connecticut, 06511. This service is for the use of physicians seeking locations, as well as physicians seeking associates, and is without charge.

From the

Connecticut Regional Medical Program

The following is an interview conducted by a CRMP staff member with William F. Bauer, Jr., M.D., general practitioner, anesthesiologist, member of the Emergency Department of Middlesex Memorial Hospital, and currently full-time director of the hospital's Shore Line Clinic and Laboratory, located in the Centerbrook section of Essex. The Clinic, open every day of the week from 8:00 A.M. to midnight, serves the seven-town Lower Connecticut Valley estuary area of Chester, Clinton, Deep River, Essex, Killingworth, Old Saybrook, and Westbrook. It was established in recognition of a growing physician shortage in the area. The hospital reports a current physician-to-population ratio in the area of 72 per 100,000 in contrast to 119 per 100,000 for Connecticut as a whole, and the average age of practitioners in the area to be 57 as compared to a national average of 47 years. CRMP has approved a hospital request for a $20,000 grant to help support the services in 1970 of Dr. Bauer and Mr. Theodore Horowitz, Director of Planning.

Q. *What Services Does the Clinic Offer?*

The Clinic is really an ambulatory care center. We offer primary diagnosis—evaluation, if you will; on-the-spot treatment, emergency care, and/or referrals. We do not encourage return visits by the patient. We encourage him to receive on-going care by a private physician. An exception would be to remove sutures or when the patient's own physician is out of town and not signed out to another physician.

Q. *What Kind of Staff Will You Have?*

There will be an experienced—and I stress this—an experienced, licensed physician on duty during all hours that we are open. There will also be two RN's and a radiologic technician on duty at all times. Other paramedical personnel will be on hand as needed. Laboratory personnel will work the normal 8:00 A.M. to 4:00 P.M. hours weekdays and a half day on Saturdays, but in case of need the hospital's laboratory services are only 15 minutes away by courier.

Q. *How About Equipment?*

We're completely equipped to act as an emergency room. We're also equipped for minor surgery. We have endotrachial sets, positive pressure oxygen equipment, monitor-cardioverter-defribilator units, 300 MA X-ray equipment, X-omat processing, and courier service to the hospital for supplies or, for example, emergency X-ray. And of course we have full laboratory service.

Q. *Do You See the Clinic Operation Benefitting the Physician?*

Yes. The doctors in this area are doing an excellent job. They have my admiration. But statistics show there is shortage of doctors here. People complain they are not receiving the medical care they desire or have to travel to get it. We can help with the load. We can take emergency cases off their backs. A doctor can sign out to us, if he has to go away for a few days. He can also see his patients here to cut down travel time for both parties. And he can treat his emergency cases here rather than his own office, utilizing our equipment and nursing personnel.

Q. *What About Fees?*

There is a minimum charge of $8.00 for use of the facility, equipment and services of paramedical personnel. On top of that there is a charge for dressings, supplies, drugs, appliances—the ordinary charges a patient would get in the hospital.

There is a separate minimum charge to the patient of $10.00 for professional services of the physician on duty. That charge can be greater for special services, such as suturing a laceration. The scale is in line with the CMS fees for those services. Our schedule of minimum charges is pegged above that for a private office visit so that we won't be in competition with anyone.

Q. *Where Will You Find the Physicians to Staff the Clinic?*

I hope they'll be local practitioners. I've had inquires from three local physicians so far. I also hope to find some retired physicians living in the area who would be willing to work here part-time. One such man, a surgeon, came in, looked around the clinic, and took an application. I hope to hear from him again.

Q. *Will the Clinic Aid in Recruiting Physicians to the Area?*

I think it will. The area will be more attractive to a man or woman in any specialty because of the facilities and equipment available at the Clinic and because, in the absence of a working arrangement with another physician, he or she can sign out to the Clinic.

Q. *What Are Your Duties?*

The delivery of medical care is my principal responsibility. I will take care of patients during Clinic hours. My other duties are administrative and planning, though the latter will not occupy much time in the immediate future.

Q. *What About the Future?*

We're sticking our toe in the water—trying things out. We can fail or we can be pioneers in this aspect of health care delivery. In about a year we'll take a hard look at the operation to see what we've accomplished and where to go from there. Right now we're trying to get the people and the doctors to appreciate the Clinic and use it.

Placement Wanted

OPHTHALMOLOGIST—49 years of age, Certified, wishes solo type practice in Connecticut. Presently in practice, Military obligation completed.

INTERNIST—31 years of age, Certified with National Boards, wishes solo or group type practice in Connecticut. Presently in practice. With Connecticut license.

PEDIATRICIAN—39 years of age, Certified with Connecticut license, wishes institutional type practice in Connecticut. Available now.

OPHTHALMOLOGIST—39 years of age, Certified with National Boards, wishes solo or associate type practice in Connecticut. Presently in practice. Military obligation completed. Available anytime.

INTERNIST—34 years of age, Eligible, wishes to practice in Connecticut. Military obligation completed.

PATHOLOGIST—38 years of age, Certified, wishes group type practice in Connecticut.

SURGEON—33 years of age, Certified with National Boards, wishes group or associate type practice in Connecticut. Presently in practice. Available immediately.

GENERAL PRACTICE—59 years of age, Eligible with Connecticut license wishes group, associate, institutional or industrial type practice in Connecticut. Available immediately.

INTERNIST—36 years of age, Eligible with National Boards, presently in practice wishes solo type practice in Connecticut. Available in the fall.

THORACIC AND CARDIOVASCULAR SURGERY—36 years of age, presently in practice, wishes group or associate type practice in a large community in Connecticut. Primarily interested in thoracic and cardiovascular surgery but would be interested in combining this with general surgery. Available immediately.

ANESTHESIOLOGY — 45 years of age, Eligible with National Boards, wishes group, associate, institutional or industrial type practice in Connecticut. Available immediately.

ANESTHESIOLOGY—37 years of age, Eligible, presently in practice, wishes solo, associate or group type practice in Connecticut. With Connecticut license. Available immediately.

INTERNIST—33 years of age, Eligible with National Boards, wishes group or associate type practice in Connecticut. Available in October.

OPHTHALMOLOGIST—31 years of age, Certified with National Boards, wishes solo, group or associate type practice in Connecticut. Available immediately.

INTERNIST—36 years of age, Certified with National Boards, wishes group or associate type practice in Connecticut. Available in August.

INTERNIST — ENDOCRINOLOGY — 33 years of age, Eligible with National Boards. Prefers to practice internal medicine-endocrinology in a group or with associate, but must affiliate with university-type teaching hospital. Military obligation completed. Available immediately.

FAMILY PRACTICE—55 years of age, Certified with National Boards, wishes group or institutional type practice in Connecticut. Available immediately.

PEDIATRICIAN—35 years of age, Certified, wishes group, associate or institutional type practice in Connecticut. Available immediately.

PATHOLOGIST—31 years of age, Certified with National Boards, wishes group, associate or institutional type practice in a large or medium size community in Connecticut. Available immediately.

Placement Opportunities

CONNECTICUT-SENIOR PSYCHIATRISTS—in a 3-year accredited dynamic, decentralized community-oriented mental hospital. Affiliated with Yale University, Wesleyan University, and University of Connecticut. Excellent opportunities for professional growth and advancement. Salary commensurate with experience and training. Psychiatrist I, $19,303; Psychiatrist II, $20,128; Psychiatrist III, $21,911. Liberal benefits. Eligibility for Connecticut license required. Send all particulars in first letter, including references, to Mehadin K. Arafeh, M.D., Superintendent, Connecticut Valley Hospital, Box 351, Middletown, Connecticut 06457.

EMERGENCY ROOM—Full-time preferred in 250 bed Bristol Hospital. General Practitioner or specialist. To join 3 full-time plus part-time physicians rendering 24 hour medical coverage to 55,000 community. Excellent, new facilities, nursing and specialty backup. Salary plus liberal benefits for full-time. Call or write Richard P. Fredericks, Administrator, Bristol Hospital, Brewster Road, Bristol, Connecticut 06010. Telephone 589-2000.

VACANCY FOR A PART-TIME PHYSICIAN—to serve as District Medical Consultant in Putnam. Duties involve essentially reviewing medical reports, ascertaining disabilities, and advising vocational counselors in related medical matters. Connecticut license required. One hour per week. Job would be particularly interesting to physicians who are phasing out current private practice. For further information, please contact Mr. Clay White, District Supervisor, Connecticut State Division of Vocational Rehabilitation, Norwich District Office, 257 Main Street, Norwich. Telephone 887-3546.

PATHOLOGIST—part time for the Masonic Home and Hospital, Wallingford, Connecticut. Attractive, well paying, steady and not much time consuming position.

WANTED—Third man for Family Practice, no investment, salary if desired, equal time off, new 120-bed hospital next to office, Northern Connecticut, 15 miles from Hartford. J. Kristan and L. O'Connor, M.D., 57 Union Street, Rockville, Connecticut 06066.

OPENING FOR INTERNIST in 496 bed State Veterans Hospital—$21,911-$26,729—plus 6% adjustment October 1970. Many fringe benefits. Write or call Personnel Officer, Veterans Home and Hospital, Rocky Hill, Connecticut, 529-2571, Extension 395.

PHYSICIAN—part time; to work mornings in the office only. Practice limited to general medicine and aviation medicine. For further information contact, James E. Crane, M.D., 965 Hope Street, Stamford, Connecticut.

PSYCHIATRIC RESIDENT, PHYSICIANS, PSYCHIATRISTS—positions available at Norwich Hospital. Community oriented, geographically unitized hospital wth mainy forward-looking, exciting programs. Fully approved for three years psychiatric residency training with NIMH grants available. Resident's salaries begin at $10,690 and all salaries will be increased by 6% in October, 1970. Many fringe benefits. Write Superintendent, Norwich Hospital, Norwich, Connecticut 06360.

OBSTETRICS & GYNECOLOGIST—Third man needed, board-eligible or certified, with military obligations completed, to join two other physicians in Middletown. Starting salary $18,000; partnership after three years. Congenial stall, University town. Prospective applicants are encouraged to write to Donald E. Miller, M.D., 18 Crescent Street, Middletown, Connecticut.

OFFICE-HOUSE for sale. Connecticut shoreline area. Seven room office fully equipped—x-ray and lab. Excellent opportunity for immediate income from active, lucrative, practice. Close proximity to Yale-New Haven Medical Center. Physician recently deceased. For details write to: P.O. Box 222, Clinton, Connecticut 06413.

PEDIATRICIANS—Two Pediatricians are needed to serve a growing community of over 50,000 people. Area consists of several small towns with population of 3,000 to 14,000 each. Good country living with easy access to larger cities via well developed highway system. Community hospital is now expanding and more physicians are needed. Contact: E. B. Raheb, Chief of OB & GYN, Day Kimball Hospital, Putnam, Connecticut 06260.

PATHOLOGIST ASSISTANT—Board qualified or eligible. Attractive newly established position available in a progressive 320 bed accredited general hospital located in beautiful Southern Connecticut. Clinical and anatomic pathology. Expanding hospital laboratory with approved school of medical technology. Salary open, excellent benefits. Please send curriculum vitae to: Gilles Allard, M.D., Pathologist, Director of Laboratories, St. Joseph's Hospital, Stamford, Connecticut 06904.

CONNECTICUT-SENIOR PSYCHIATRISTS—In a 3 year accredited dynamic, decentralized community-oriented mental hospital. Affiliated with Yale University, Wesleyan University, and University of Connecticut. Excellent opportunities for professional growth and advancement. Starting salary range $19,303-$26,986, depending on experience and training. Liberal benefits. Eligibility for Connecticut license required. Send all particulars in first letter, including references to Mehadin K. Arafeh, M.D., Superintendent, Connecticut Valley Hospital, Box 351, Middletown, Connecticut 06457.

PSYCHIATRISTS AND PSYCHIATRIC RESIDENTS—Openings in the mental hospitals and mental health clinics of the State of Connecticut. Residencies, $10,694-$16,110; Psychiatrist I, $19,303-$23,755; Psychiatrist II, $20,128-$24,700; Psychiatrist III, $21,911-$26,729. Excellent benefits and opportunity for advancement. For further information contact Mr. Robert Tacey, Agency Personnel Administrator, Department of Mental Health, 90 Washington Street, Hartford, Connecticut.

PHYSICIANS AND RESIDENT PHYSICIANS—opportunities with the State of Connecticut in medical hospitals, institutions for the mentally retarded, and Veterans' Home and Hospital. Residencies $10,694-$16,110; Physician $17,760-$21,960; Senior Physician $19,303-$23,755; Maternal and Child Health Physician $21,002-$25,700; Medical Consultant $21,002-$25,700; Internist $21,911-$26,729; Chief, Epidemiology Section $21,911-$26,729. Excellent benefits. For further information contact Mr. John Crowley, Agency Personnel Administrator, Department of Health, 79 Elm St., Hartford, Connecticut or Mr. Edmund Buetsch, Personnel Officer, Veterans' Home and Hospital, Rocky Hill, Conn.

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ANYONE INTERESTED IN THE ABOVE IS ASKED TO CONTACT THE EXECUTIVE DIRECTOR'S OFFICE, 160 ST. RONAN STREET, NEW HAVEN, CONNECTICUT 06511.

In Memoriam

Duennebier, Harold William, Tufts Medical School, 1940. Dr. Duennebier was a general practitioner in the New London area since 1946. He served in the U.S. Army Air Force Medical Corps from 1942-1945. Dr. Duennebier was a medical staff member at Lawrence Memorial Hospital, New London, and was a member of the New London County Medical Association, the American Medical Association, the American Academy of General Practice and the Connecticut State Medical Society. Dr. Duennebier died June 26, 1970 at the age of 54.

Iasiello, Emilio P., Naples Medical School, 1946. Dr. Iasiello was a general practitioner in the Bridgeport area since 1955. He served on the staff of St. Vincent's Hospital in Bridgeport, and was a member of the Fairfield County Medical Association, the Connecticut State Medical Society, and the American Medical Association. Dr. Iasiello died June 4, 1970 at the age of 48.

AMERICAN BOARD OF FAMILY PRACTICE

The American Board of Family Practice announces that it will give its SECOND examination for certification in various centers throughout the United States. The examination will be over a two-day period on February 27-28, 1971. Information regarding the examination and eligibility for the examination can be obtained by writing:

Nicholas J. Pisacano, M.D.,
Secretary-Treasurer
American Board of Family Practice, Inc.
University of Kentucky Medical Center
Annex #2, Room 229
Lexington, Kentucky 40506

PLEASE NOTE: Deadline for receiving completed applications in the Board office is *November 1, 1970.*

AROUND THE STATE

New Haven County

Board of Governors
New Haven County Medical Association

The Board of Governors of the New Haven County Medical Association met at Rapp's Paradise Inn in Ansonia, Connecticut on Wednesday, June 17, 1970 with President Steward J. Petrie presiding.

Much of the meeting was devoted to the "blue ribbon panel" Ad Hoc "Himler-Budd" Committee Report. This Committee, with Dr. Saul Milles as chairman consisted of: Saul S. Milles, Chairman, New Haven; George A. Bonner, New Haven; Jerome K. Freedman, New Haven; J. Wister Meigs, New Haven; John Moench, New Haven; Richard Rosenthal, Branford; David S. Fischer, New Haven; Bernard A. Burnham, Waterbury; Gordon MacLeod, New Haven; Ira Goldenberg, New Haven; Matthew Campione, Meriden; Elliott S. Mayo, Waterbury; William E. Swift, New Haven; John B. Atwater, New Haven; Howard Spiro, New Haven and David F. Musto, New Haven.

Following two amendments to Doctor Milles' report, New Haven County completed its task of analyzing the Himler-Budd Report and was able to forward its recommendations to the Council, AMA Delegates, and the New England Assembly in time for the June AMA annual meeting. The Association took a certain amount of pride in this accomplishment, and those responsible were duly acknowledged by their peers on the Board of Governors.

The matter of responsible fees charged by responsible doctors was discussed and the probability of public disclosure of the existence of the New Haven County Medical Association peer Review Committee and the reasonable fees charged by New Haven County members was also discussed and should soon be resolved.

Except for the Himler-Budd Report about AMA reorganization and reorientation, the most urgent item revolved about the rather confusing topic of "Health Care Planning". The basis for further action in this field was outlined by the Board of Governors. Several Board of Governors task forces have been activated to engage in meaningful involvement in innovative and comprehensive—yet compassionate and perceptive—relativity to the needs of the individual and the community—both at large and singularly—as they reflect upon the ultimate, as well as the day to day aspirations of the medical care consumers within the "system". The Board of Governors felt that our Comprehensive Health Planners are much in need of help and indicated their desire to give them all the help they need in the days to come.

The "delivery of health care system" the "health care industry", and the "new system for health care delivery" will thusly be assured of the assistance of the practicing and dedicated physicians of the New Haven County Medical Association in *the search* for better ways of bringing better health care to all of our citizen consumers in today's organized planned community.

The various New Haven County Medical Association committees who have been working on a variety of tasks, will report their findings in September. At that time, the next report will be made. In the meantime, happy holidays to all of our readers during the summer vacation.

Respectfully submitted,
William L. West, M.D., *Clerk*

News from Yale University School of Medicine

Dr. Milton J. E. Senn, the famous "children's doctor" at Yale, will retire after serving on the faculty here since 1948.

His career as a pediatrician, child psychiatrist, and teacher has made him one of the pioneers in his field, and his numerous writings, including columns in magazines, have made him a family advisor to millions of parents.

Dr. Senn is 68, the University's retirement age, but he will continue at Yale as Emeritus Professor and will also become Vice President for Child Studies of the Field Foundation of New York City.

He has been Sterling Professor of Pediatrics and Psychiatry at the Yale School of Medicine, and was Director of Yale's famed Child Study Center from 1948 to 1966. He also served as Chairman of the Yale Pediatrics Department from 1951 to 1964.

At Yale Dr. Senn's interests have focused on the American child and his family, including the training of numerous pediatricians, psychiatrists, educators and social scientists to be able to help children. A recent symposium in March, 1970, on the disadvantaged child held in honor of Dr. Senn at Yale attracted many of his most famous former pupils from government and university positions.

WOMAN'S AUXILIARY

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Mrs. John J. Mendillo, North Haven

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A pageant of fashion depicting the role of women through history, and twenty-one "Show and Tell" exhibits were two of the highlights of the 47th annual convention of the Woman's Auxiliary to the American Medical Association. More than 1,000 physicians' wives attended the June 21-25 meeting at the Drake Hotel in Chicago.

Auxiliary president Mrs. John M. Chenault of Decatur, Ala., presided over the sessions.

On Sunday, June 21, the Auxiliary sponsored a reception honoring Mrs. Chenault, president, and Mrs. R. C. L. Robertson of Houston, Tex., president-elect.

The convention formally opened on Monday, June 22, with a keynote address by Mrs. Louise Bushnell, director of women's activities for the National Association of Manufacturers.

Mrs. Bushnell offered a "Challenge to Women in the '70s" by calling on them to find answers to the world's greatest problems. "Let's clean the cerebral cobwebs, first out of ourselves, and then out of others," she said. She asked the women to strive to make freedom work and added that the majority of communities could be improved greatly by discipline and understanding.

"Snob appeal is another cerebral cobweb," she continued. "We should not show prejudice of any kind—by tone, facial expression or word."

"Most certainly we do not need to be liberated by any group of our sisters. You who are leaders where you live . . . stand tall and let your action speak louder than your words," Mrs. Bushnell concluded.

Gerald D. Dorman, M.D., 1969-70 AMA president, was the guest speaker at the "Heavenly '70s" luncheon honoring AMA officers, trustees and wives. Following the luncheon Mrs. Chenault presented a check for $498,950.69 to Robert C. Long, M.D., president of the American Medical Association Education and Research Foundation.

The contribution represented an increase of $70,000 over last year. Mrs. Chenault noted that physicians' wives contributed a total of $4,196,083.46 to the foundation since the Auxiliary adopted the project in 1951.

The Tuesday luncheon honoring national past presidents and honorary members featured the unique fashion show. Presented by the sponsors of the Community Homemakers Home Health Aid Service, Inc., of Kenosha, Wis., the fashion show originated about a year ago when several medical auxiliary members were discussing the desperate need for temporary household help for families when the homemaker is ill or disabled.

In the afternoon there was a special session on drug abuse presented by Russel Deter, M.D. of El Paso, Tex., husband of the newly-named chairman of the health careers committee for the national Auxiliary.

A resolution on health care of the poor was passed on Wednesday, June 24. The resolution stated:

> WHEREAS, the House of Delegates of the American Medical Association, at the 1969 convention, adopted a resolution promoting a program on health care of the poor; and
>
> WHEREAS, the resolution recognizes the basic right of every citizen to have available to him adequate health care; and
>
> WHEREAS, the resolution recommends that the medical profession, using all means at its disposal, endeavor to make good medical care available to each person, therefore
>
> RESOLVED, that the Woman's Auxiliary to the American Medical Association recommend that the Program Development Committee implement

this program on Health Care of the Poor to include Indian, migrant and ghetto care.

In her inaugural address, Mrs. R. C. L. Robertson said because "service in the seventies" should be the goal, the focus of the Auxiliary this next year will be on the responsible adult in the health picture. "We hope that each Auxiliary member will consider it her responsibility not only for her own and her family's good health, but for the promotion of positive good health for the people of her community," she commented.

In concluding her remarks, Mrs. Robertson urged Auxiliary members to accept responsibility for the promotion of better health in the community and to be aware of their neighbors' needs.

Drugs for Reducing Increased Intracranial Pressure

Markedly increased intracranial pressure can cause headache, vomiting, edema of the optic disks, alterations in behavior, impairment of consciousness, changes in vital signs and, if unrelieved, death. Emergency measures are required, including, where possible, removal of the cause of the increased pressure.

Among the common neurosurgical disorders leading to increased intracranial pressure are severe head trauma, intracranial neoplasm, subtentorial and intracerebral hemorrhage, cerebral edema and infarction, and sinus thrombosis. The medical disorders that can cause increased intracranial pressure include Addison's disease, vitamin A intoxication, inadequate respiratory exchange with consequent excess of carbon dioxide in the blood, hypertensive encephalopathy, toxemia of pregnancy, generalized edema due to renal, cardiac or hepatic disease, hypervolemia, acute meningoencephalitis, cerebral malaria, and acute alcoholism. Reduction of increased pressure obviously requires management of the primary medical disorder. Several drugs can cause or aggravate raised intracranial pressure; among them are nalidixic acid (NegGram), tetracyclines (in infants), isoniazid, and corticosteroids when large doses are used or therapy is prolonged.

Emergency Treatment

Spinal tap can be used to relieve increased intracranial pressure in patients with meningeal infections, but where an intracranial mass may be present, spinal tap can be hazardous; it can cause herniation of the cerebellum or other subtentorial brain tissue through the base of the skull, with compression of the brain stem and death. Dehydrating measures such as restriction of water intake and the use of diuretic agents can safely lower increased intracranial pressure when the increase is the result of medical disorders, but such measures can be dangerous in patients suffering from trauma or other neurosurgical disorders.

Diuretic Drugs

Parenteral administration of hypertonic solutions of mannitol or urea or the oral administration of glycerol is effective in reducing increased intracranial pressure because of their osmotic effects. Cerebral edema due to head trauma is more effectively reduced by controlled hyperventilation measures (to reduce hypercapnia), and occasionally by hypothermia; osmotic diuretics which effectively reduce intracranial pressure usually do not reduce the brain swelling seen after head trauma or cerebral anoxia.

Mannitol

Mannitol is less active osmotically than urea, but it is less likely to induce a rebound increase in intracranial pressure, and it is not contraindicated in patients with renal disease. The usual dose is 1.5 to 2 Gm of mannitol per kg of body weight given intravenously in a 15% solution (Abbott; Travenol) or a 20% solution (Travenol) over a period of 10 to 15 minutes. This dose lowers cerebrospinal fluid pressure significantly for three to eight hours. (For additional comments on mannitol diuresis, see The Medical Letter, Vol. 10, p. 5, 1968.)

Urea

As the use of mannitol to reduce cerebrospinal fluid pressure has increased during the last few years, the use of urea (Ureaphil—Abbott; Urevert—Travenol) for this purpose has decreased considerably. It is still used for some patients, however. The usual dosage range employed by most Medical Letter neurosurgical consultants is 0.5 to 1.5 Gm of urea per kg of body weight; sterile lyophilized urea is used. It is administered as a 30% solution. Doses within this range, administered intravenously at a rate of 20 to 60 drops per minute, reduce the cerebrospinal fluid pressure for three to eight hours. The use of urea is contraindicated in patients with severe impairment of renal, hepatic, or cardiac function, marked dehydration or active intracranial bleeding.

Glycerol

Glycerol is a useful oral osmotic agent in neurosurgical procedures, especially where a prolonged increase in intracranial pressure is expected (G. Cantore et al., J. Neurosurg., 21:278, 1964). It is non-toxic and is partly metabolized, yielding 4.32 kilocalories per Gm. The patient can take it by mouth, with lemon juice to make it palatable, or it can be administered by nasogastric tube. A dose of 0.5 Gm/kg reduces intracranial pressure within 30 to 60 minutes. One to 2 Gm/kg can be administered initially, with a maintenance dose of 0.5 to 0.7 Gm/kg every three to four hours. M. Buckell and L. Walsh (Lancet, 2:1151, 1964) recommend 75 ml by mouth, one to three times a day.

Glucocorticoids

Many neurosurgeons use parenteral corticosteroids to prevent and treat cerebral edema surrounding focal cerebral lesions or resulting from severe head trauma, but some Medical Letter consultants doubt that the corticosteroids are effective. Their value in preventing or reducing cerebral edema has not been established by controlled trails.

Conclusion

The management of increased intracranial pressure caused by neurosurgical procedures has been improved by the use of osmotic diuretics. Increased intracranial pressure due to medical disorders is treated primarily by measures designed to control the disorders. Some drugs can cause or contribute to elevated intracranial pressure or cerebral edema.

Reprinted from the Medical Letter on Drugs and Therapeutics, New York, N.Y. Vol. 12, No. 11, May 29, 1970.

News From Yale University School of Medicine

The Griffin Hospital in Derby, Conn., and the Yale School of Medicine have signed an affiliation agreement according to a joint announcement today by A. J. DeLuca, administrator of the hospital, and Dean F. C. Redlich of the medical school.

"With the signing of this agreement the hospital moves closer to fulfillment of its long-range goal, the development of a comprehensive community health center in the lower Naugatuck Valley" Mr. DeLuca stated.

Dean Redlich noted that he "looks forward to a closer relationship between Yale and the Griffin Hospital. This agreement provides the foundation upon which both parties can work together to achieve common health objectives."

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SPACE DIETS IN MEDICINE

On June 12, 1970 the fourth annual William J. H. Fischer Memorial lecture was held at the Milford Hospital. The speaker was Dr. Henry T. Randall, Professor of Surgical Research at Brown University School of Medicine and Surgeon at Rhode Island Hospital. Dr. Randall was introduced by Dr. Louis H. Nahum who described Dr. Fischer's contributions to medicine and to Milford Hospital.

Dr. Randall opened his talk on the completely synthetic, bulk-free "space diets" by reviewing the history of parenteral alimentation. Parenteral glucose was first proposed as a substitute for food intake in the late 1890's and as early as 1915 Murlin and Rich and Yamakawa introduced the use of fat emulsions for intravenous feeding. In the late 1920's whole blood and plasma were added to the physician's armamentarium and in 1939 Elman first proposed the use of protein hydrolysates. The classic work of W. C. Rose on essential amino acids in man and the work done on parenteral nutrition by Elman, Brunschwig, Rhodes, Moyer, Lockwood, Marchese, and others, laid the groundwork for the utilization of completely parenteral alimentation in man. F. D. Moore's basic research into the nutritional problems of the surgical patient certainly is a cornerstone in the technique of replacement of oral intake in complex surgical patients. Recently Dudrick, Wilmore, and Rhodes introduced the infusion of hypertonic solutions through a large central venous catheter for the long-term nutrition of debilitated patients.

Completely synthetic, chemically refined, and bulk-free diets soon were proposed for the replacement of parenteral alimentation in patients who were acutely ill or who had severe gastrointestinal disease. In 1965 Winitz reported 15 volunteers who ingested only such a diet and distilled water for periods of up to 19 weeks. This work was supported by N A S A because of its practical application to the feeding of space explorers and thus these diets became known as "space diets."

It was soon noted that there were no ill effects from ingesting this diet and there was a striking reduction of fecal output to one small bowel movement every 5-6 days. There was a progressive fall in cholesterol level of the blood. A cubic foot of a 75 per cent solution was able to produce 2,830 calories per day for a month. Thus, it had the added advantage of complete flexibility in composition, of total absorbability, with virtually no digestion being required, and, it could be stored in a small space.

Such diets were then suggested for medical use by George Cahill among others. Dr. Randall then presented illustrative cases of the practical application in the management of patients who suffered from malabsorption or were severely disabled by extensive surgery on the gastrointestinal tract. He showed that, with such a diet, they were able to maintain positive nitrogen and potassium balance in a patient who had had near complete resection of the small bowel following a mesenteric infarct. These diets are marketed commercially as Codelid and Vivonex. Briefly, the diet consists of glucose, essential amino acids, macro and trace minerals, and water- and fat-soluble vitamins excepting vitamin K. The diet has been used as a complete alimentation in certain patients with the use of a microdrip and a Baron pump through a small nasogastric catheter and has the added advantage of not plugging the lumen. Dr. Randall was successful in using it as a dietary supplement in patients who had marked weight loss due to difficulty in metabolising their oral feeding and for the exclusive nutrition in patients with severe diseases of the gastrointestinal tract.

The speaker stressed the possible indications in ulcerative colitis, malabsorption syndrome, pancreatitis, intestinal fistulas, peritonitis, sepsis, and in acute and severe trauma. He also added a warning that it should never be used over 25 per cent weight by volume, and one should slowly build up the desired calories over a period of several days in order to take advantage of the adaptation of the patient's gastrointestinal tract. Elemental diets are an intermediate step between high-caloric parenteral feeding and normal food intake. They have the advantage of ease of absorption, minimal digestion, adjustable composition, low bulk, high caloric value, and are presumably non-antigenic. The disadvantage of this diet is the high osmolality, the poor taste, the lack of vitamin K, the slight regurgitation risk in some debilitated patients, and the necessity for frequent small or continuous feedings.

G. S. Parrella, M.D.

MEETINGS

The information on this "meetings" page is offered as a service to all specialty groups and allied health agencies in order to publicize postgraduate educational opportunities available to subscribers. The deadline for publication in Connecticut Medicine is the tenth of the preceding month, i.e., the tenth of September for the October issue. Send copy to: Connecticut State Medical Society, 160 St. Ronan Street, New Haven, Connecticut 06511.

August 25—Tuesday 3:00 P.M.

Neuropathology Conference

Danbury Hospital

Gilbert Solitaire, M.D., Associate Professor of Pathology, Yale Pathology Department

August 26—Wednesday 3:00 P.M.

EKG Interpretation Conference

Danbury Hospital

Nathaniel Selleck, M.D., EKG Department

September 1-3—Tuesday-Thursday

The American College of Physicians Course on Dermatological Diagnosis and Treatment For the Internist

University of Maryland School of Medicine, Baltimore, Maryland

Contact: Edward C. Rosenow, Jr., M.D., F.A.C.P., Executive Director, American College of Physicians, 4200 Pine Street, Philadelphia, Pennsylvania 19104.

September 9-11—Wednesday-Friday

The American College of Physicians Course on Renal Diseases: Pathophysiology, Diagnosis and Management

Mayo Graduate School of Medicine, Rochester, Minnesota

Contact: Edward C. Rosenow, Jr., M.D., F.A.C.P., Executive Director, American College of Physicians, 4200 Pine Street, Philadelphia, Pennsylvania 19104.

September 16—Wednesday

Pediatric Urology—Nephrology Symposium

Yale University School of Medicine

Contact: Robert M. Weiss, M.D., Section on Urology, Yale University School of Medicine, 333 Cedar Street, New Haven, Connecticut 06510. (Telephone 203-436-1574).

September 25-26—Friday and Saturday

Postgraduate Course for Pediatricians

"Disorders of the Spleen in Childhood", Yale University School of Medicine, Department of Pediatrics

Speakers: Drs. Howard Pearson, Lawrence Pickett, Norman Talner, Joseph Bertino

Contact: T. F. Dolan, Jr., M.D., Department of Pediatrics, Yale University School of Medicine, New Haven, Connecticut 06510. (Telephone 203-436-8388).

October 5—Monday 8:00 P.M.

Lecture: Problems of Abortion

Hartford County Medical Association, 230 Scarborough Street, Hartford, Connecticut

Speaker: Keith P. Russell, M.D., Clinical Professor of OB & GYN, U.C.L.A.

This lecture will be part of the "Ladies Night" program. Physicians, their wives and guests are welcome.

November 18—Wednesday

Perinatal Seminar

Mary S. Harkness Auditorium, Yale Medical School

Speakers will include: Dr. Alex Minkowski, Director of the Centre de Recherches Biologiques Neonatales, Paris, France. Two discussions: "The Biochemistry of the Small for Dates Infant" "The Pediatrician and the Problem of High Risk Pregnancies".

Richard Banfield, M.D., and Ruth Wilf, Ph.D., Discussion on various aspects of a prepared child birth program.

Panel Discussion on Neonatal Intensive Care and Transitional Care of the New Born Infant:

Moderator: Robert H. Usher, M.D., Neonatal Unit and Royal Victoria Hospital, Montreal, Quebec, Canada.

Alexander Campbell, M.D., Assistant Professor of Pediatrics and Director of the Neonatal Unit at Yale University School of Medicine.

Stanley James, M.D., Columbia University College of Medicine. Jeryl Gagliardi, R.N., New Born Intensive Care Unit, Yale-New Haven Hospital.

Contact: Robert L. Harris, M.D., 581 Farmington Avenue, Hartford, Connecticut. (Telephone 203-232-5202).

Science News

Cancer In Connecticut, 1966

(*Conn. Health Bulletin:* May 1970, Christine, B. W., Sullivan, P. D., Connelly, R. R.) Cancer continues to be one of the two leading health problems. It is the second leading cause of death in Connecticut, as in the entire nation accounting for 169.2 deaths per 100,000 persons in 1968 as compared to 354.1 due to heart disease.

The impact of cancer on an individual in terms of the threat it represents to the normal life span will depend on such factors as the primary site of the tumor, extent of the disease at the time of diagnosis and promptness of treatment. The age at which the tumor occurs is an important related factor. That is, a woman stricken in 1965 with cancer of the breast at age 57, the median age for female breast cancer, could have looked forward to an additional 14 years of life, based on the current life expectancy at that age.

On the other hand a male with cancer of the prostate could have expected only 12 additional years of life in the absence of the disease, based on the median age at diagnosis of 71 years.

Cancers of the digestive tract and lung, bronchus and trachea accounted for over half of all the male cancers in 1966 while tumors of the reproductive organs accounted for a similar proportion in females.

The early detection of cancers in non-invasive stage as that of cervical cancers in situ was seen to be accompanied by a decrease in incidence of invasive lesions of that site.—L.H.N.

United States War Losses In Vietnam

(*Statistical Bulletin,* December 1969) By Jan. 1, 1970 United States battle deaths in the Vietnam War had passed 40,000. This is a seventh of the United States battle losses during World War II. The heaviest losses of our Armed Forces in Vietnam were suffered in February and May 1968. In each of these months, more than 2000 battle deaths were reported.

Of the total battle deaths, 31 per cent occurred in the Marine Corps, 64 per cent among Army troops, 2 per cent in the Air Force and 3 per cent among Navy personnel.

Over the same period 1961-69, non-battle deaths from disease and non-battle injuries totalled more than 7000.

The percentage of the wounded in Vietnam who survived after reaching medical facilities has been about 97.5 per cent, which is appreciably higher than the 95.5 per cent registered in World War II. —L.H.N.

Identification Of Excess Cardiovascular Risk

(*Minn. Med.:* 52, 1217, 1969, Dawber, F. B.) Certain constitutional and environmental traits relate to development of coronary heart disease (CHD). These are overt disease, a symptomatic myocardial ischemia and diseases associated with a high rate of CHD such zanthomatosis diabetes mellitus, gout and hypothyroisism. In addition are those patients with increased levels of serum lipids, elevated blood pressure, elevated hemoglobin, or hematocrit levels, decreased vital capacity, physical inactivity and excess weight.

These characteristics can all be readily determined by the physician in his office and can serve as a basis for selecting the population at excess risk on whom preventive measures may be applied.

Proof of benefit of changing "risk factors" has not been established yet. Nevertheless therapy aimed at producing desirable change appears reasonable.—L.H.N.

Behavior Patterns And Personality Characteristics Related To Prevalence Rates Of Coronary Heart Disease In American Monks

(*Jr. Chronic Dis.:* 22, 91, 1969, Caffrey, B.) Benedictine priests who are omnivorous had the highest rate of myocardial infarction. They were described as sensitive extroverts. The results are in keeping with the general theory that some intrapersonal conflict between emotional and rational elements may be important in the etiology of coronary heart disease.—L.H.N.

Effect Of Low-Nicotine Cigarettes On Angina Pectoris

(*Ann. Inter. Med.* 71, 599, 1961, Aronow, W. S., Swanson, H. J.) These authors exercised 10 male smokers after smoking low-nicotine cigarettes. Smoking increased systolic blood pressure heart rate, but no ischemic ECG change.

Of the 40 exercise ECGs, 24 were positive in both the smoking and non-smoking state.

Those patients with coronary artery disease who exercise after smoking even low-nicotine filter cigarettes may be unable to meet the increased demand for myocardial oxygen caused by an increase in blood pressure and heart rate. As a result angina develops sooner.—L.H.N.

Reappraisal Of Papillary Muscle Dysfunction

(*Amer. J. Med.:* 46, 862, 1969, Shelburne, J. C., Rubinstein, D., Gorlin, R.) Fourteen patients with papillary muscle dysfunction were evaluated clinically and studied by right and left heart catheterization selective coronary arteriography and left ventricular cineangiography.

The murmur was found to vary in timing from early to late systole or to be holosystolic. The site, radiation and intensity of the murmurs were inconstant.

There was precise correlation between timing of onset of regurgitation by ventriculography and timing of the murmur within systole.

There was no characteristic ECG pattern.

All patients had severe coronary artery disease but with an increased incidence of severe right coronary artery lesions.

Abnormal left ventricular systolic contraction was found in all but one of the patient groups, so that this could be as much a cause of a burden on left ventricular function as was the mitral regurgitation.—L.H.N.

Blood Pressures And Risk Of Coronary Heart Disease: The Framingham Study

(*Dis. Chest.* 56, 43, 1969, Kannel, W. B., Schwartz, M. J., McNamara, P. M.) Hypertension is a common major contributor to CHD mortality. Blood pressure contributed to risk even in the absence of other conditions such as obesity, gout, abnormal lipids, diabetes, and ECG abnormalities.

The study extended over 14 years and embraced 5,127 subjects. Every clinical manifestation including angina, coronary insufficiency, myocardial infarction and sudden death was distinctly and impressively related to both systolic and diastolic pressure.

Risk was proportional to the level of blood pressure. Labile blood pressure elevation may contribute to risk as well as fixed hypertension since risk was strikingly related to blood pressure levels. —L.H.N.

Treatment Of Arrhythmias In Myocardial Infarction

(*Arch. Inter. Med.:* 124, 101, 1969, Zipes, D. P.) The reduction in mortality from acute myocardial infarction is due almost entirely to detection interpretation and treatment of arrythmias. The therapeutic guidelines include quick transportation of the patient to a monitoring facility, aggressive management of early electrical or hemodynamic disorders, control of hypoxia, electrolytes, hyperglycemia, hypotension or pH imbalance.

Lidocaine is used I.V. for premature ventricular beats, 1-2 mg/kg I.V.

If ventricular tachycardia or fibrillation appears direct current cardioversion is mandatory. If ventricular ectopic beats occur in a slow heart rate, atrial pacing will often eliminate them.

If atrial arrhythmias occur then digitalis is indicated. At times cardioversion will be effective. Complete heart block requires transvenous pacing. First degree heart block usually resolves spontaneously.—L.H.N.

Rethinking Coronary Thrombosis Lessons From Experimental Therapeutics With Anticoagulants

(*Med. J. Aust.* 2, 425, 1969, Lovell, R. R. H.) A study of the modes of death in patients surviving the acute stage of infarction who die in the next few years show that about half die of recurrent infarction and the other half are sudden deaths.

In the latter group no recent changes in the coronary arteries are found. If the patient is on anticoagulants his risk of sudden death is not diminished.

These considerations indicate 2 approaches to secondary precaution. One is a drug which will prevent or diminish platelet adhesiveness. This presumably should reduce reoccurrence of thrombosis. The other is to detect those patients with ectopic beats and treat them with antiarrhythmic drugs. The hope is to avoid sudden death from an arrhythmia.—L.H.N.

Orotidinuria Induced By Allopurinol

(*Science*. 168: 861, May 15, 1970, Fox, R. M., Royse-Smith, D., O'Sullivan, W. J.) The administration of Allopurinol to patients suffering from hyperuricemia and to normal subjects results in increased excretion of the pyrimidine nucleoside orotidine.

Evidence is presented for the interference by allopurinol of the de novo biosynthesis of uridine 5'-phosphate in man.—L.H.N.

Control Of Sulphur Oxide Emissions

(*Science*, 168, 1076, May 29, 1970) The emission level of sulphur oxides resulting from the use of sulphur-bearing fuels to generate electrical energy will be more than 4 times as great by the year 2000 unless immediate action is taken to control the problem.

There is no commercially proven technology for control of such sulphur oxides which are second only to automobile emissions as a cause of air pollution.—L.H.N.

Inadequate Student Financial Aid

(*Science*. 168, 1076, May 29, 1970) The National Association of State Universities and Land-Grant Colleges has revealed that financial aid offices on campuses across the nation are running out of money long before all student requests have been filled.

Michigan State and Ohio State Universities report they were forced to refuse approximately 1500 requests each. The situation is due to increasing aid requests, spiraling college costs, slowdown in federal funding, reluctance of banks to make loans under the Guaranteed Student Loan Program and the failure of some state legislatures to provide adequate appropriations.—L.H.N.

Bell Laboratories

(*Science*. 168: 1076, May 29, 1970) Bell Laboratories is getting out of the missile defense business after it finishes its current contract on the Safeguard Anti-Ballistic Missiles.

Bell wants to shift its 16,000 personnel working on the ABM into civilian areas.—L.H.N.

York's Biggest Mistake

(*Science*. 168, 1076, May 29, 1970) Herbert York, former research chief in the Pentagon under Eisenhower, once believed that some chemical and biological weapons, especially the nonlethal variety, could be usefully incorporated into our defense arsenals and might, in some degree, make war more humane.

"I have come to realize that the situation is much more complicated than I had first thought it was. Indeed these weapons generally make war more inhumane, especially when used in conjunction with conventional weapons.

"I consider my earlier support of biological and chemical weapons to have been perhaps my biggest mistake of that period."—L.H.N.

NEW BOOKS IN REVIEW

DUNCAN's DISEASES OF METABOLISM. ENDOCRINOLOGY AND NUTRITION. 6th Edition. Edited by Philip K. Bondy, M. D. W. B. Saunders Company, Philadelphia, Pa., October 1969. Volume I, 710 pp with 330 illustrations. Volume II, 667 pp with 264 illustrations. 34 Contributors. $39.00.

Reviewed by: LOUIS H. NAHUM

Duncan's Diseases of Metabolism was a classic for 5 editions, outstanding and everyone came to rely on it as a valuable source of information. In this Edition, Edited by Professor Philip Bondy of Yale there are two volumes, one on genetics and metabolism and the other on endocrinology and nutrition. The 34 authors who have contributed to these two volumes are experts in their field, but one can see the guiding hand of the editor in the remarkably even style and simple and clear presentations of highly complex subjects.

The various chapters were written from the point of view of basic principles and facts derived from them. As a reference book and for teaching exercises it could not have been more felicitously written. Clinical complications are overt and correct in each chapter and technics for studying individual problems in the areas of these volumes are most rewarding.

While not all chapters conclude with a summary of their contents, they all have a suitable list of references for those wishing to pursue further individual points in each chapter.

An innovation are addenda published at the end of the book after the index. Science moves very rapidly so that even a thoroughly up to date presentation becomes outmoded by the time it has passed through the process of publication. What does not change frequently are the fundamental principles underlying the data with which a book deals. To minimize the importance of the time which has passed since the chapters were written, each author has been offered an opportunity to write an addendum to his chapter to make it as current as possible. It is these addenda that will be revised with each printing of the book to make the newest copies as nearly correct as possible.

A glance at these addenda show how little the main body of the text needs modification and how carefully the authors wrote in basic principles which change very slowly.

Connecticut Medicine

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Wyeth Laboratories	551, 552

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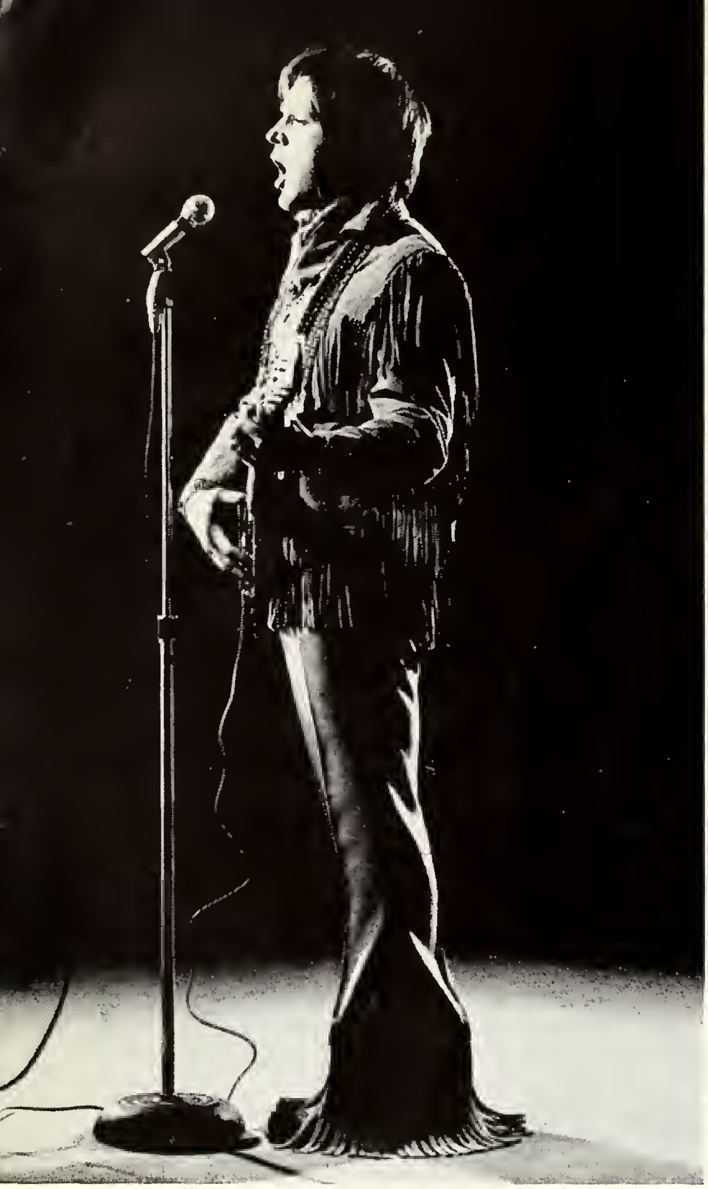

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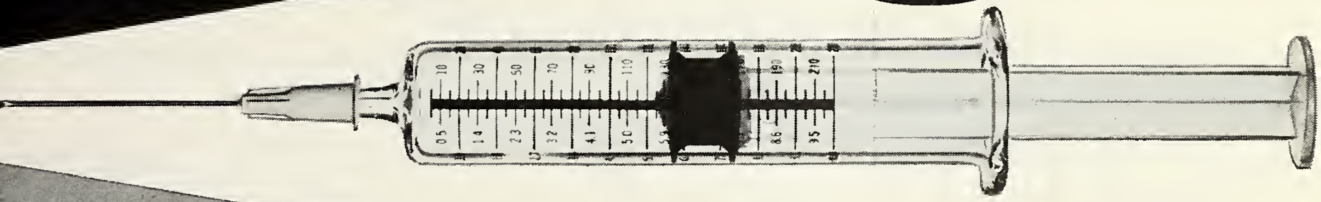

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CONTENTS

editorials

Hunger And Malnutrition In The United States 601
Psychiatric Disorders In The Community 602
The FDA: Harnessing The Scientific World For Its Important Cause 605
Earth Day—April 22, 1970 607
Compensation For Time And Skill Versus Compensation for Procedures 608
Infusion Thrombophlebitis 610
Psychopathology Of The "Pill" And Wishful Thinking . . . 611
The Doctor And The Dying Patient 613
Sex Determination Reconsidered 616
Vaccines Against Pneumonia—Going From Cure To Prevention 617

scientific

Technical Aspects Of Surgical Management Of A Right Hepatic Artery Aneurysm, *Allan L. Toole, M.D., Harold Stern, M.D., Samuel Lerner, M.D., and Robert Lowman,* M.D. 619
Management Of Complications Of Pancreatic Pseudocysts, *J. Vilinskas, M.D.* 622
Surgical Correction Of Congenital Coronary Defects, *John A. Ogden, M.D.* 626
Acute Arthritis Of The Sternoclavicular Joint Due To Coliform Bacillus, *Allen F. Delevett, M.D., and David T. Monahan, M.D.* 629

departments

The President's Page 631
From The Executive Director's Office 633
Special Article—Medicine In Israel, *Ned Thomas* 644
Electrocardiogram-Of-The Month, *Hyman N. Chernoff, M.D.* 646
Medical Grand Rounds—Yale-New Haven Hospital, *Frederick Lee Sachs, M.D. and Lewis Landsberg, M.D.* 649
Law-Medicine Notes, *J. Alfred Fabro, M.D.* 654
Correspondence 656
    Thoughts On A Book Review
    Emergency Admission In Hospital Utilization
Physician's Placement Service 660

miscellaneous

New CSMS Staff Members 638
Council Approves Position Paper On Delivery Of Medical Care For The State Of Connecticut 639
Doctor's Office 655
Connecticut Regional Medical Program 659
In Memoriam 662
Meeting Notices 663
Science News 664

Connecticut Medicine

editorials

Hunger And Malnutrition In The United States

Malnutrition is here as reported by the Citizens' Board of Inquiry and by the CBS television program, "Hunger in America". But what is the incidence, severity, and location of malnutrition? Not all malnutrition is caused by dietary inadequacy, because it can also be secondary to infestation with intestinal parasites which cause anemia and also secondary diarrhea.

Hunger has been reported particularly among hard-to-reach rural inhabitants of the Southeast and along the Appalachian Mountains, Indian Reservations, among migrant farm workers and also among people living in city slums. Recluses and incapacitated elderly people who must fend for themselves may also experience hunger. Although it is estimated that one-third to one-half of the very poor may experience hunger of varying intensity, there is no truly reliable estimate of the number of hungry people in our country.

In all likelihood, malnutrition is much more prevalent than hunger per se, but it is not as politically dramatic. Malnutrition producing physiological impairment is probably common. Conditions such as iron deficiency, growth impairment, and obesity are wide-spread. Formerly, scurvy and beri beri were common. Now goiter and rickets have been reported in alarming proportions. So much so that Congress directed HEW to conduct a survey to identify the incidence, magnitude, and location of malnutrition and related problems within the United States.

Dr. Arnold E. Schaefer, Director of the National Nutrition Survey, presented preliminary findings from surveys in Texas and Louisiana. The common finding is malnutrition from iron, vitamin A, vitimain C, iodine, protein and calories. These same nutrients are in short supply also among poverty people in American cities and disadvantaged rural people. There was found an appalling rate of dental decay, missing teeth or filled teeth. Dental hygiene was dismal. While dental pathology does not result from inadequate nutrition, it is certainly closely associated with diet.

Nearly 10 per cent of the survey population in Texas had discernible goiters. Iodized salt which prevents it was not generally used. In fact 40 per cent of the markets failed to stock iodized salt. An additional finding from the two surveys was low height in relation to age among preschool children.

The U.S. Department of Agriculture in its most recent survey in 1965 of food habits of 6,200 households, revealed that half had diets that failed to meet the recommended dietary allowances. Most often below allowance was calcium, vitamin A, and Vitamin C. About one fifth of the diets provided two thirds or less of the recommended dietary allowance of these nutrients.

Classical malnutrition exemplified by vitamin deficientcy diseases is but a small segment of the spectrum. The less dramatic manifestations such as growth retardation, weight loss, increased burden of chronic diseases, depression, weakness, retarded convalescence from disease, poor performance in pregnancy, are widespread and of great significance. What could also be a serious individual and social problem is impaired brain and central nervous system development associated with protein malnutrition of the mother and after the child born.[1]

Thus the groups in danger of malnutrition are infants, preschool children, the elderly and pregnant women, in particular when the pregnancy occurs during very early adolescence or when pregnancies are closely spaced. In these latter instances, both the mother and child are in jeopardy because of inadequate nutritional preparation for the pregnancy and inadequate nutritional support during pregnancy.

Poverty is not alone in the causation of malnutrition. Other factors are illness, ignorance of the relation of diet to health, indifference to the importance of good nutritional practice, loneliness, and mental illness. There are numerous causes of malnutrition which are secondary to cancer, gastrointestinal disorders, febrile diseases, and biliary and pancreatic diseases.

The nutrition program surveys discovered examples of almost complete ignorance regarding the need for appropriate food sources of certain nutrients, for example, table salt as a source of iodine. Ignorance, indifference, and poverty combine to expose the child to the risk of malnutrition. Even though he may not demonstrate clinical symptoms of malnutrition, the individual may have undesirably low levels of vitamins and minerals in his tissues and is, therefore, without any significant nutrient reserve.

It has been firmly established that the preschool-aged children are most vulnerable to the effects of malnutrition. For example well documented is the synergism between malnutrition and infectious disease. Infections in the undernourished are more devastating, persist longer, and result in a much higher death rate. Obviously infectious diseases themselves play an important role in the initiation of malnutrition itself. Nutrient deficiencies sometimes result also from drug therapy and surgery. This reflects, of course, the inadequate attention to nutrition as well as the lack of awareness of nutritional complications on the part of the physician. In fact, all such deficiency disorders can be prevented had the patient and the physician utilized proper understanding of nutrition and diet.

Iron deficiency is found in large numbers of children and is very frequent among women of all ages. In women the deficiency is aggravated by menstrual losses and by the extra requirements of pregnancy and lactation. Parasitic infestation and iron deficiencies account for some of the deficiencies among children in the South.

Obesity is also a form of malnutrition resulting from a combination of excessive caloric intake and inadequate caloric expenditure. It has been estimated that almost 40 per cent of the American population are obese. Ironically, malnutrition bordering on starvation has resulted from ill-advised weight reduction programs (crash programs) frequently used by adolescents and young women. The harmful effects of malnutrition on the individual an dsociety are incalculably great.

L.H.N.

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Psychiatric Disorders In The Community

A recent estimate based on findings in general practice in Britain disclosed that psychiatric disorders were present in 20 per cent of cases, but only a minority had entirely psychiatric diagnoses. Thus the community survey by Goldberg and Blackwell[1] as well as that reported in the *British Medical Journal*[2] have disclosed psychiatric problems of previously unsuspected dimensions. In particular were the minor affective discorders, phobic states, drug dependence, alcoholism and organic brain syndromes in the elderly. Apparently the hospital services deal with only a small fraction of patients with these conditions and the great majority are either treated by the family physician or remain untreated.

The commonest disturbances encountered are anxiety and depression. Their management raises questions of practical importance. How do they present their problem to the physician? How can these patients be detected? How and by whom should they be treated? How effective is their management and how can this be improved? One would suppose that these patients who had entirely psychiatric diagnoses would be the most important to recognize because they may very well be those that will require the collaborative service of a psychiatrist. The difficulty is that only a minority of patients with true emotional disorders present exclusively with

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I adore this house.
My in-laws are great.
The neighbors are wonderful.

Indications For use in management of anxiety and tension occurring alone or as accompanying symptom complex to medical and surgical disorders and procedures. Though not a hypnotic, fosters normal sleep through antianxiety and related muscle-relaxant properties

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Important Precautions. Carefully supervise dose and amounts prescribed, especially for patients prone to overdose themselves. Excessive prolonged use has been reported to result in dependence or habituation in susceptible persons, as alcoholics, ex-addicts, and other severe psychoneurotics After prolonged excessive dosage, reduce dosage gradually to avoid possibly severe withdrawal reactions Abrupt discontinuance of excessive doses has sometimes resulted in epileptiform seizures

Warn patients of possible reduced alcohol tolerance, with resultant slowing of reaction time and impairment of judgment and coordination.

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Side Effects include drowsiness, usually transient; if persistent and associated with ataxia, usually responds to dose reduction; occasionally concomitant CNS stimulants (amphetamine, mephentermine sulfate) are desirable. Allergic or idiosyncratic reactions are rare, but such reactions, sometimes severe, can develop in patients receiving only 1 to 4 doses who have had no previous contact with meprobamate. Previous history of allergy may or may not be related to incidence of reactions Mild reactions are characterized by itchy urticarial or erythematous maculopapular rash, generalized or confined to groin Acute nonthrombocytopenic purpura with cutaneous petechiae, ecchymoses, peripheral edema and fever have been reported. One fatal case of bullous dermatitis following intermittent use of meprobamate with prednisolone has been reported. If allergic reaction occurs, meprobamate should be stopped and not reinstituted Severe reactions, observed very rarely, include angioneurotic edema, bronchial spasms, fever, fainting spells, hypotensive crises (1 fatal case), anaphylaxis, stomatitis and proctitis (1 case) and hyperthermia Treat symptomatically as with epinephrine, antihistamine and possibly hydrocortisone. Aplastic anemia (1 fatal case), thrombocytopenic purpura, agranulocytosis and hemolytic anemia have occurred rarely, almost always in presence of known toxic agents. A few cases of leukopenia, usually transient, have been reported on continuous administration.

Meprobamate may sometimes precipitate grand mal attacks in patients susceptible to both grand and petit mal. Extremely large doses can produce rhythmic fast activity in the cortical pattern. Impairment of accommodation and visual acuity has been reported rarely. After excessive dosage for weeks or months, withdraw gradually (1 or 2 weeks) to avoid recurrence of pretreatment symptoms (insomnia, severe anxiety, anorexia). Abrupt discontinuance of excessive doses has sometimes resulted in vomiting, ataxia, tremors, muscle twitching and epileptiform seizures. Prescribe very cautiously and in small amounts for patients with suicidal tendencies Suicidal attempts have resulted in coma, shock, vasomotor and respiratory collapse and anuria. Excessive doses have resulted in prompt sleep, reduction of blood pressure, pulse and respiratory rates to basal levels; and occasionally hyperventilation. Treat with immediate gastric lavage and appropriate symptomatic therapy. (CNS stimulants and pressor amines as indicated). Doses above 2400 mg./day are not recommended.

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psychiatric symptoms. Most of them have somatic complaints which obscure the underlying affective disorders. In this situation their psychiatric illness is hidden and the physician may not be aware of their real disturbance.

This may happen in a number of ways. In the first place, somatic concomitants of anxiety such as palpitation, precordial pain, shortness of breath, and the somatic concomitants of depression, such as inertia, lassitude and malaise, all can simulate physical disease. In the second place anxious people prone to hypochondriacal introspection may become occupied with somatic sensations which pass unheeded in normal people. An anxiety reaction triggered off by an overt and wholly organic complaint may pass unnoticed against the background of the physical disease. Clearly the physical and psychological facts of the clinical picture need to be sorted out in each case.

The reason that such patients did not easily come to light is that most patients presented a physical complaint and the psychiatric disturbance did not come to light in the 10-15 minutes available for the interview. The majority of the "hidden psychiatric" patients formulated their problems in somatic terms not only to the doctor but also to themselves. It needed direct inquiry to elicit the phenomena of psychiatric illness, especially because the patients did not see themselves as emotionally disturbed. Why did such patients behave this way?

Goldberg and Blackwell interpreted this in three related ways: The patient may have learned that doctors deal primarily with physical illness so he thinks the doctor expects him to produce physical complaints. A second reason is that the patient had his symptoms for some time, but is now going through a time of emotional distress, so his symptoms seem worse. The chronic pain seems worse when the patient is distressed. Many patients may feel that it is more socially acceptable to be physically than emotionally ill and fear the stigma of being thought of as a "psychiatric case". The fact is that some doctors as well as patients consider that a stigma attaches to patients who are psychiatrically ill and until this is no longer the case, many patients are likely to continue to formulate their problems in somatic terms. The prejorative label "neurotic" has died hard.

Most of the illnesses seen in the survey were in fact minor affective illness and formal psychiatric illness was unusual. Depression was found not only ubiquitous, but to respond well to treatment. Most of the psychiatrically ill patients were not "entirely psychiatric" and had physical complaints in association with their psychiatric disturbance. It follows that not only is psychiatric disturbance common among patients visiting their doctors, but that it is often present in those who confront their doctors with physical symptoms only. If a person is still ill after six months, it turns out that they tend to have insoluble life problems such as sick relatives or long standing personality disorders and it was the circumstances to which the depression was reactive that was intractable.

As the community becomes more informed and articulate there will be increasing demand for psychotherapy from sympathetic and experienced physicians. It follows that expert training will be necessary to ensure that the psychotherapy practice is both constructive and helpful. What could be of help in this regard is greater emphasis in the curriculum on psychological and social aspects of medicine.

In the meantime more research is needed into the factors which influence outcome and into the indications for different therapeutic methods. Regular contact between physician and psychiatrist can be of mutual benefit both in hospital and family practice. It would seem appropriate to extend this approach more fully. Most patients are dealt with by their family doctors who will in turn be better able to provide adequate care if he is skilled to recognize and deal with the psychological factors that are inextricably connected with physical symptoms.

L.H.N.

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The FDA: Harnessing The Scientific World For Its Important Cause

One of the most important and certainly the most newsy of the regulating agencies in the United States is the Food and Drug Administration (FDA). There is every sign that its reputation which was badly damaged by the ungainly feature of the pantomine proceedings banishing cyclamates on October 18 will be redressed by the new Commissioner Dr. Charles Edwards.

Given that the most serious arguments against the use of cyclamates is that their efficiency as aids to weight reduction is still in doubt, the question still remains why was the banishment of cyclamates undertaken in such unseemly haste. Can it ever be good government that an important decision affecting not merely the property of manufacturers, but the peace of mind of a large part of a very large population, should be made on a Friday afternoon and made public on a Saturday? Would it not have been better to have waited for time to plan an announcement that would seem less a response to panic. Would there not have been a case for waiting for more convincing results than those on which the decisions was taken. That the FDA should have allowed outsiders, even powerful outsiders, to use its machinery for doing this is reprehensible even if this forgiveable.

Another case in point is the recent furor over the use of tolbutamide to relieve diabetes. It has received criticism never far from dormant that the FDA does not take sufficient precautions to prevent the press from first unveiling to the public premature reports of the results of clinical trial of drug efficacy. Patients have been unnecessarily alarmed by reading about the possible harmful effects of drugs even before doctors have been informed. Doctors particularly are concerned with what action the FDA proposes to take to prevent future reports from seeing the light of day before doctors have been informed.

The way in which the FDA should seek to deal with the safety of drugs and foods is one of the questions provoked by the Fountain Committee of Congress inquiry in the middle of June. There is very little doubt that Dr. Edwards is right in saying that the first task is to restore a sense of pride to a battered agency. What he might have added is that it is important that some method should be found for assessing more objectively the biological hazards of new chemicals. The hazards on which attention is now concentrated are not the outright poisons but rather the materials whose effects are necessarily covert and slow.

In the assessment of the risk of using this or that chemical, there is bound to be a period when experimental evidence first accumulates when it is exceedingly hard to interpret this evidence. In effect this is the reason given by the FDA for not acting sooner on cyclamates. Now we know it would have been quite proper to have waited much longer. The problem then is what to do in the period before any suspicion about a drug can be fully tested. It would be quite a boon for the public peace of mind, if the FDA were now publicly to resolve to take a measured view of the evidence substantial or otherwise. What does this imply for the Delaney amendment, the form of words by means of which Congress has sought to put an end to cancer.

The real practical problem is how is the amendment to be applied, what kind of evidence is to be taken as proof that some food stuff may be carcinogenic. Is there to be a ban the instant a tumor appears in an experimental animal? What does Congress require for a test of significance in the comparison between a group of experimental animals and the controls. Is the probability of chance occurrence less than 0.5 sufficient to outlaw some previously unsuspected chemical? Or will Congress wait until the evidence justifies a more certain conclusion.

Another difficulty in the administration of this legislation is the means by which the F.D.A. should combine its judicial and its scientific functions. No one seems fully to recognize the intellectual difficulty of the judicial function. If there is anything to be learned from the unseemly taking of the decision on cyclamates and on the package insert for oral contraceptives, it is that the quasi-judicial proceeding of the FDA should be made more formal. Other regulatory agencies of the Federal Government have several commissioners to share responsibility and it is hard to see why the FDA should not move at least a good distance in that direction by appointment of an old-fashioned council to solemnize decisions and to share responsibility for them. Without such an instrument properly constituted by Congress each successive Commissioner will find himself intolerably squeezed between the bureaucracy of HEW and the imitators of Mr. Ralph Nader.

The FDA needs also more rational definition of the functions of its scientific work, the origin of which can be found in the simple days when the acme of vigilance was the identification of unsuspected contaminants in ordinary food-insect parts in flour was a perennial favorite. The task in short was the enforcement of regulations already in force. The novelty in the past few years has been the way in which the FDA has also assumed some of the public responsibility for seeking out those agents in the environment, natural as well as artificial, which may be suspect.

The trouble, of course, is that, however hard it tried the FDA will never be able to do everything that might be tried. For turning over every stone can raise a host of unexpected problems. The FDA scientific branch will be able only to tackle a small part of what needs to be done if mutagenesis and teratogenesis as well as more tests are to be applied to the ingredients of ordinary life. But if the FDA cannot be at once judge and detective agency, where should it concentrate? The more urgent need, of course, is that the FDA should be strongest in the determination of the criteria on which safety and danger are determined.

What this implies is that the FDA should be skilled at defining the protocols which should be satisfied by the tests which manufacturers carry out and that it should be most of all concerned to advance the techniques by means of which these tests can be applied. At the same time, it should beware of being panicked whenever the prospect of danger is raised. The danger is that too rapid investigation with inadequate resources may serve only to confuse the issue as with the cyclamates. In the long run, it would appear that the FDA's best hope is that by the judicious placing of contracts with outside researchers and by the stimulation of a professional interest in this important work, the FDA can more effectively harness the scientific world for its important cause.

There remains the most glaring need and the least readily acknowledged of all the FDA shortcoming, its tendency to act independently of what happens elsewhere. The U.S. must avoid becoming the largest intellectual island in the world. What is the reason for anyone believing that manufactured chemicals such as 2.4.5-T herbicide acts differently in the U.S. than in Europe or Asia? Is there no means by which assessment of the hazards of drugs, food additives and other potentially hazardous materials may be carried out internationally? Why does the FDA set the danger of mercury in rivers and lakes at 0.5 per million when WHO sets it at .05 per million?

If Dr. Edwards wishes to make a constructive mark on the FDA he will seek not merely independence from the Secretary of HEW, but also a much closer working relationship with comparable organizations in other countries and in the World Health Organization.

L.H.N.

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Earth Day—April 22, 1970

The Observance of Earth Day on 22 April could mark the launching of a mass movement on behalf of the environmental protection and a better quality of life. Thus, in all probability, it represents a major change that has occurred over the past year in public perception of environmental problems. It is not surprising then that many students have found the environmental issue to be related to nearly all of their concerns, such as the Vietnam War, racial injustice, dehumanizing aspects of urban life, and the failure of both government and business to behave in a manner broadly representative of the public interest.

Environmental Teach-In, Inc., the national ad hoc student organization that promoted the observance of Earth Day, is being re-incarnated in a more militant form, known as Environmental Action. This group will encourage and use such tactics as lawsuits, proxy fights, demonstrations and campaigns for or against political candidates. Earth day observances were said to have been conducted by some 4000 local groups, half of them, campus groups and half, organizations of labor, Women League of Voters, conservation groups and other community groups. Nearly all intend to remain active and will be the national organization's principal source of strength.

Only a few years ago most who considered themselves conservationists were still concerned principally with such problems as the protection of the Grand Canyon from dam builders and the protection of the Cascade Range from miners and lumbermen.

The genesis of the idea of Earth Day is not easy to establish, but it was in the air. Through their writings and appearances on the campus lecture circuit, Rene Dubos and other biologists such as Barry Commoner of Washington University, LaMont Cole of Cornell, and Paul Ehrlich of Stanford, have been energetically sounding the warning that the earth itself may become uninhabitable. Now, finally, the concept of "spaceship earth" is, without doubt, another idea whose time has come.

A year ago, there was little evidence of public concern about domestic population growth as a major factor in environmental degradation, although there has long been an awareness of a "population crisis" in the less developed countries. A major theme of Earth Day was the warning that unless the U.S. population was stabilized and a "zero growth rate" achieved, nearly all environmental problems will be exacerbated and eventually made insoluble.

Another significant change in the perception of environmental issues by the public is that now there is increasing awareness that effective environmental action is impossible without a reordering of national priorities. A cliche always handy to the tongue of Earth Day speakers was that the United States cannot fight in Vietnam, build the supersonic transport (SST), explore the moon, lace its cities with freeways, and overcome air and water pollution too.

In an Earth Day speech in Denver, Senator Gaylord Nelson, with whom the idea for an environmental teach-in on April 22 originated, put it this way: "Earth Day can—and it must—lend a new urgency and a new support to solving the problems that still threaten to tear the fabric of this society—the problems of race, of war, of poverty, of modern-day institutions. Ecology is a big concept—not a copout."

The people who are most likely to be blamed for a copout are the leaders of the Nixon Administration and the leaders of both parties in Congress, according to Luther J. Carter, if the federal government does not soon take action stronger than anything now underway to stop environmental degradation. Reinemer[2] has recently pointed out that the Budget Bureau has specifically refused to include on its advisory committees representatives of the Consumer Federation of America. The Committee—The National Industrial Pollution Control Council is composed of board chairmen or presidents of major oil, automobile, electric utility, mining, timber, coal, airline, manufacturing companies, plus presidents of the U.S. Chamber of Commerce, the National Association of Manufacturers and the National Industrial Conference Board. In other words the countries' polluters.

The President's choice for Chairman of the Council is Bert Cross, board chairman of Minnesota Mining and Manufacturing. His company still has not complied with a 1966 state order in Wisconsin to stop discharging sulphurous waste into municipal sewers. In short, the President's Council headed by Cross is composed exclusively of polluters.

Informed ecologists, old-fashioned conservationists, vocal students, or "silent majorities" are not represented, nor do they have separate advisory councils. They are excluded at the Presidential and the Bureau of Budget levels. The guardians of the people's interest can get their information from industries' anti-pollution advertisements!

Inside the White House and the red brick executive office building of the Bureau of Budget, the "rabbits guard the wilting lettuce". Earth day will have to do a heroic task to see to it that the government will now act to revise existing boards.

L.H.N.

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Compensation For Time And Skill Versus Compensation For Procedures

Since 1950 the pace of scientific medicine has quickened almost beyond belief. Much emphasis is laid today on the importance of team work in medical care. The team approach is everywhere, in the operating room, in the research laboratory, in the developing of special skills. However, in the worst medical crisis, the patient often looks desperately for one person on whom he can rely and the threatened submergence of the personal physician in favor of the team, may make this person difficult to identify.

A senior colleague once said that his most humbling experience had been when a dying patient told him that when he came into his room, it was like a light shining in the darkness. Surely this is testimony enough to the enduring need for a personal physician not only with a reverence for life but with the ability to see the wood for the trees in this day of complex medicine. It means that there must be a willingness to take the time and trouble with individuals at the expense of that abstraction known as the patient.

The physician, however, must live and the question arises how one can place a satisfactory monetary value on his professional medical services. It is well known that this is almost impossible. Nevertheless, it is attempted by the Federal government. Through its medicare and medicaid programs the United States Government does have an opportunity through its remuneration for services to dictate the quality and types of services rendered patients. This fact has apparently not been fully appreciated until recently. However, Senator Magnuson is aware of this and in a statement before the Subcommittee on Executive Reorganization of the Committee on Government Operations expressed himself clearly as follows:

> "Basic to a consideration of medical costs is the professional fee structure of medicine. I suggest that the fee structure is unsound and itself contributes to excessive costs. Fee structures are heavily weighted towards encouraging procedures rather than time and skill. Surgically oriented third party fee structures are the norm. Doing something to a patient pays. Talking with him does not. A doctor can receive $35.00 for taking 5 minutes to sew up a cut, but would be considered daring to charge $12.50 for a half hour counseling session. This inequality may force many physicians to perform procedures. . . . The quality of medicine could be improved at lower cost to the public were physicians adequately compensated for their time and skill rather than for procedures. Reform of the fee schedule in Federally sponsored programs in cooperation with the medical profession would be one place to start".

Further emphasis of the importance of our Government's role in such matters is indicated by the values accepted by the Social Security Administration for services and procedures under the Medicare Program. For example, a doctor can earn more money by ordering a vectorcardiogram which has little established clinical value and requires no time of his own than he receives for an office or clinic visit which should and normally does require a great deal of his own time for talking to his patient, carefully examining him, and counseling him, the most important part of good practice.

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A review of this list of accepted charges displays many and even more glaring examples of inappropriate emphasis on values by monetary evaluations. Recognizing human nature it requires very little imagination to realize the response of physicians in practice to the Government's attempt to set the fees for their services with such a sense of values. The master clinician cannot but feel such action by the Government impossible to understand.

Perhaps it is such establishment of unrealistic monetary values on the practice of medicine that will inhibit and discourage good medical practice and contribute to reducing the effectiveness of medical practice. Such facts reveal major deficiences in medical education, emphasis on time and fees for services which influence the quality of practice lay and professional. It is no wonder that taking a careful history, performing a good physical examination, and taking time with patients and their families are so blatantly neglected when even our government values them so little.

A major problem of modern medicine is that the patient can easily get lost in the scientific comuplexities of a case or as Sir Francis Walshe said in 1950 in his Linacre lecture entitled, "Humanism History and Natural Science in Medicine". He had a conviction that to rebuild a bridge between medicine and the humanities is a pressing need; that the building can be done only from the side of medicine and that someone must make a start if medicine is not to lapse into a mere congeries of techniques, to fail in coherence on its theoretical side, and to suffer the loss of its traditional values.

What the government is doing in its valuation of medical services can only hasten the day when the personal physician will be replaced by a mindless team and thereby the profession will suffer the loss of its traditional values.

L.H.N.

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Infusion Thrombophlebitis

Almost every patient in intensive care units in a hospital have an intravenous catheter for infusion of medications and antibiotics. Such treatment is often associated with local complications such as tissuing of the infusate and infusion thrombophlebitis. This requires either abandonment of the infusion or reintroduction of the catheter elsewhere in the body.

Several factors have helped substantially to reduce the danger of earlier technique: plastic infusion sets, and presterilized intravenous plastic cannula. But some factors remain to produce local complications. One is the duration of the infusion. In 1960 Aldman and Garsten found infusion thrombophlebitis in 88 per cent of their cases. It appears that the first 8 hours of the infusion is relatively safe from phlebitis. After the first 8 hours, the incidence rises steeply. The veins of the hand seem to be more subject to thrombophlebitis than those in the antecubital fassa.

When plastic sets were introduced in place of red rubber ones the incidence of thrombophlebitis dropped markedly. The high incidence of thrombophlebitis in Page's series of 1952 was due to the type of tubing used. He tested buffered and nonbuffered 5 per cent dextrose solutions. In 1961 Skajaa found no difference in incidence of thrombophlebitis using 3 different sizes of needles and no difference between various plastic giving sets. However, if the needle is left in a vein without an infusion being given, the incidence of thrombophlebitis is very low even after 72 hours.

The type of infusion is related to the incidence of thrombophlebitis since it is decreased if the pH of the solution being infused was raised to neutrality. Of the various drugs used in infusions, hydrocortisone produced a decrease in incidence of infusion thrombophlebitis whereas heparin did not. Five per cent glucose, normal saline and blood were about equal on their effect on thrombophlebitis. Anesthetic agents seemed not related, but then the heparin infusion continued for less than 8 hours.

Hastbacka et al, in 1966 in a very large series found the incidence to be twice as great in females.

Brown[1] found an overall incidence of infusion thrombophlebitis in 27 per cent of his 158 infusions in 100 patients. The incidence of infusion thrombophlebitis in the first 24 hours was only 8 per cent and rose to 18 per cent on the second day. The largest rise in cases of infusion thrombophlebitis occurred during 24-48 hour period. It would, therefore, seem indicated that if intravenous infusions have to be maintained for more than 24 hours, the site of infusion should be changed at 24 hour intervals.

Brown found that antibiotics when added to the infusion was accompanied by a low incidence of thrombophlebitis. This raises the question of whether antibiotics should be used prophylactically in infusions which have to be maintained in one site for more than 24 hours. Such a question, however, is complex and needs further controlled trials.

All factors examined except for hypertonic solutions did not seem to influence markedly the incidence of infusion thrombophlebitis except the factor of time. If the site of infusion were to be changed every 24 hours, the problem of infusion thrombophlebitis would be almost eliminated.

L.H.N.

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Psychopathology Of The "Pill" And Wishful Thinking

The contraceptive pill is by now being blamed for a lot of things. It may be that some of the blame is unjust. One should be particularly suspicious of reports of psychopathology linked to the use of this contraceptive agent. In fact, doubt has been cast on the nature of the relationship between contraception and the depression or migraine that follows its use. Two authors have recently reviewed the psychopathology of the pill and have pointed out how open some of the questions still are.

Musaph, a Dutch psychiatrist starts out with the positive side. A woman on the pill can be expected to appreciate the relief from fear of unwanted pregnancy conferred by this medication. She will thus be better able to enjoy intercourse as a result of enhanced libido. Surveys on this point, however, indicate that in only about half of these women is libido actually increased. On the other hand, libido is linked to the events of the menstrual cycle, being lessened in the progestational phase, during which there is also a greater tendency to psychiatric disorders. For this reason, interference with the cycle might affect psychological balance. A woman should be able to enjoy freedom from taboos which the use of the pill rather than mechanical devices ensures her.

The contraceptive ritual can be practiced at a time unrelated to sexual relations and this can have a greater spontaneity in consequence. A woman should enjoy being mistress of her own reproductive life. This, however, is not always the case because her total personality is concerned in the situation and it is unjustifiable to consider her alone. The entire family is involved in contraception. If the family is peaceful and normal then the pill can do nothing but good. If there is strife then the husband might react with anxiety about side effects. He may fear loss of his dominance conveyed by fatherhood. He may become impotent or indeed completely paranoid.

The wife's reactions will also depend on whether there is neuroticism in her make up. If she is already disturbed, then the pill may well upset her more. She may neglect to take her pill in a neurotic desire for pregnancy, even at a most inconvenient time. Apart from libidinal changes much has been written about side effects since Kaye[1] drew attention to them in 1963. Wallach and Garcia[2] have seen it as an expression of metabolic disorder and noted the similarity between some complications such as rise in blood pressure, headache, irritability, rhinitis, sinusitis, and the signs and symptoms of premenstrual tension. Grant[3] has pointed out, however, that before the pill, all methods of contraception were liable to fail at times. There was always a gambler's chance that pregnancy would ensue. The complete reliability of the pill, therefore, places on the woman a burden of choice

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which she never had to face before. This can lead to anxiety and depression.

Professor H. V. Zalko of Berlin sees much of the psychodynamics as related to the previous personality of the individual. He has recognized among his own patients with neuroses a number of different reactions to the pill. For example, it may release guilt feelings and the woman may react with frigidity or migraine. Indeed the use of the pill may itself be a neurotic symptom as may the promiscuity to which it can lead in some patients. He finds some women with frank anxiety reactions because they are now tempted to act out fantasies of seduction or prostitution.

Professor Zalko points out further that the safety of the pill sharpens the conflict between respectability and duty on the one hand and the desire for extramarital enjoyment on the other. He finds a third type exhibiting depressive reaction with rejection of sex and its pleasures. Here the aggression is turned upon the self and is represented by depression which may be outwardly directed and manifested in hostility to the marital partner as well as a depreciation of her own feminity.

A final category is the woman who feels that taking the pill has in some way diminished her. She is now less than a woman and this feeling gives rise to anxiety over future sterility when the pill is discontinued as well as anxiety over toxic effects. To this type, taking the pill may represent an act of destruction and cause anxiety similar to that induced by therapeutic abortion.

It is accepted that the pill has some side effects at times. Oral contraception however, is also an emotion-laden subject and it is certainly not wise to assume that all psychopathology in pill users is necessarily of pharmacologic origin. The Canadian Medical Association Journal of Jan. 31, 1970[1] tells the story that in 1969 an earnest group of South African Clergy were quite sure that the miniskirt would call forth God's judgment on their country and that the Vaan dam on which the country depends for its major water supply would not fill until the miniskirt was banned by law. The miniskirt was not banned and the Vaan dam did fill.

In 1970 some people no doubt are similarly awaiting a sign that the pill will call forth a judgment. The judgment should require that psychopharmacology must be divorced from wishful thinking.

L.H.N.

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The Doctor And The Dying Patient

The physician needs to understand as well as he can what sort of patient that he is dealing with. What is his cultural background, what kind of a family he comes from and how well knit together it is. He should know also the number and depths of the patient's relationships with others and in what stead they are going to stand him now. Will they stay with him to the end or will they remove themselves. Is the family so well knit that the patient's spouse or children will be taken care of. Particularly must the doctor pay attention to what seems to be the patient's habitual mode of defense and to his proneness and ability to denial. For a time the patient's neurotic defenses may be his best friends and there is no particular reason to rush foreward to analyze them.

Then the physician should look well at the immediate environment and see if anything needs to be done to it. If in a hospital there should be open communication between the nurses and the attending physician. It is the junior nurse generally that spends the most time with the patient and it is generally she to whom the patient will turn for comfort and even for knowledge. The situation becomes especially difficult if the doctor's communication with the patient is inadequate or even bad.

The doctor needs to bear several things in mind. Generally the patient already believes he is going to die or has a good idea of it so that the essential problem is not to decide whether or not the patient needs to be told. The patient may in fact be kind to the physician even as we are kind to him and there is always the temptation to take refuge in this. It is also necessary to remember that the patient will probably be depressed and also be suffering physically particularly if he is vomiting or has dyspnoea. Particular attention to medication may make a lot of difference especially now that adequate medication for these symptoms is available. We need to make sure that depression and grief are being distinguished from physical suffering and we need to make sure that the patient is getting medication when he needs it. Above all we must remember that the nearer the patient's death approaches, the greater is his fear of loneliness and abandonment.

The doctor needs to avoid denial in himself. There is a particular form of it that is difficult to resist, that is the fantasy that he has done all that he can for the patient and therefore that he should busy himself with more important or apparently rewarding things. The doctor can do more for the patient than just busy himself with medical and physiological correlates. What we do for the dying patient is also measured by his needs. The one thing the patient needs above all else is a continuing relationship with his doctor who undertook to help him in the first place. If his own doctor no longer comes to see him or sees him fleetingly from whom else may the patient expect comfort.

There are other things which the doctor must look for in himself and come to understand as well as he can. There is his own cultural position and his own attitude toward death. Probably this will be partly realistic but also partly neurotic and it is necessary to look carefully before deciding that we are taking positions that are as reasonable as they appear at first sight to be. The physician should attempt to understand his own habitual modes of defense. Whatever they are, they are likely to be brought powerfully into play when he is confronted with an intractable problem as approaching death. Importantly he should look at his relationship with this particular patient. There may be some guilt from therapeutic failure, anger from defeated omnipotence. Indeed the whole range of countertransferance problems may enter into the situation. It is through this filter that he will see his patient and his needs.

Perhaps the total management of the dying patient can be related to the three phases described for the cancer patient by Ruth Abrams. When the patient's condition is diagnosed he needs to be told three things in words he can understand. He needs to be told what is wrong with him, what it may possibly mean to him in the future, and what medical science has to offer him. If these three things are advanced carefully, the patient generally can make some

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reasonable arrangements and may also bring his usual defenses to the situation at whatever level he finds necessary. There is then the second stage of waiting and fearing in which all the considerations outlined above should occupy the mind of the doctor.

There is finally the stage of inevitability. In this stage the fear of abandonment, physical suffering and depression are likely to be present and it is at this stage when the doctor and nurse need all the resources they can derive from their training and their personalities. When all is over and the doctor can retreat from what has been a painful situation, the physician must then remember he has responsibilities also to the members of the family, to the nursing staff and junior colleagues. It is the present custom to pretend that situations which increase the physician's own anxiety leave him unaffected. But we need to become confident in ourselves and what we have done, confident enough so we can help the others.

L.H.N.

Sex Determination Reconsidered

In insects the male has only one sex chromosome and this is represented as XO whereas the female has two sex chromosomes which are represented a XX. However, in man and most animals both the male and female have two sets of chromosomes. In the female they are the same (i.e. XX) but in the male one sex chromosome is X while the other is smaller and is not found in the female and is referred to as the Y chromosome. The male is therefore said to have an XY sex chromasome constitution. In the female each ovum carries either of the X chromosomes but in the male each sperm carries either an X or a Y chromosome. How is it then that the Y chromosome determines maleness.

In the 1920's, C. B. Bridges[1] proposed that sex differences depend on a balance between one set of genes which determines femaleness. This theory of genic balance was based on work with the fruit fly Drosophila melanogaster in which the Y chromosome causes the sperm to be motile but does not seem to be necessary for sex determination which is controlled by the ratio of the number of X chromosomes to autosomes (other chromosomes). Accordingly with a diploid set of autosomes two X chromosomes determine femaleness, one determines a male and intersexes are possible. To explain this Bridges suggested that the X chromosome of the fruit fly contains genes which determine a female and the autosomes contain genes which determine a male. This of course was not an explanation but a theory.

This theory has been extended to man in whom, of course, intersexes are also known. It was, of course, not known what all the genes were doing. Mittwoch[2] now wishes boldly to cast away the idea of genes which determine sex and consider again the effects of the sex chromosome. She proposes the idea that the X and Y chromosome could control the differences between the sexes by differentially regulating the rate of cell division and thus the rate of development of the embryo and particularly the gonads. She has collected evidence from various sources to show that the presence of extra chromosomes can affect the quantatative differences such as the number of dermal ridges in the fingers. She believes such differences are likely to depend on rates of growth and ultimately on rates of cell division.

On the basis of her evidence Mittwoch suggests that perhaps the X chromosome reduces the rate of mitosis and the Y chromosome increases it thus affecting the embryo. In such conditions the mammalian gonad which at first is not distinguishable as male or female could develop into an ovary or testis according to its rate of development. The testis which anyway begins to differentiate before the ovaries would result if there were present forces leading to its more rapid development.

This idea that extra chromosomes whether sex or autosomes can affect rates of growth might help to explain various conditions such as Mongolism with an extra autosome. Individuals with this chromosomal abnormality are smaller at birth than babies with the normal 46 chromosomes while the condition XYY has been associated with extra tall men. This type of chromosomal abnormality occurs very rarely in the general population, whereas it seems to be not uncommon among males confined for violent or otherwise dangerous potentialities in institutions. There were nine in one institution. Daly quotes Casey et al who found twelve XYY males all over six feet tall who were classified as mentally subnormal antisocial. They discovered another four among fifty tall mentally ill antisocial patients and two more among twenty-four criminals.

Daly now has described abnormal neurological findings in twelve XYY males which he believes is the result of this chromosomal abnorality. Only one of the twelve was free of abnormal neurological signs. Two gave a history of excessive intake of alcohol while one has facial weakness and is taking dilantin for seizures. There was also association of body asymmetry with neurological abnormalities of six of these patients. Five of the twelve were mentally retarded, three were schizophrenic, and three were sociopaths.

Thus neurological deficits principally motor dysfunction may be a valuable sign in identifying affected children as well as adults. Perhaps we may find a typical pattern of development of behavior disorders and other signs of mental abnormality if we study the genetic equipment of such children. The matter of personal responsibility legally considered will loom large as we come to know more about chromosomal abnormalities in relation to effective adjustment in our society.

The question still remains if the Y chromosome regulates growth of testis and perhaps of the whole body, why do two Y chromosomes also lead to a damaged brain? Furthermore we should also learn whether the testis in these patients are excessively large. Obviously much more needs to be known about the XYY constitution to validate Mittwoch's thesis about how the Y chromosome produces maleness. L.H.N.

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Vaccines Against Pneumonia—Going From Cure To Prevention

Interest in a vaccine against pneumonia was first shown at the end of World War II when Squibb started to produce a vaccine commercially against six types of pneumococci. As penicillin came into general use, however, emphasis shifted from prevention to cure and the Squibb project was dropped. Since then vaccines have been produced on a small scale only against other causes of pneumonia namely pleuropneumonia-like organisms, several viruses none of which respond to penicillin.

In this country there are between 300,000—500,000 cases of pneumonia and about 40,000 deaths most of them caused by types of penumococci 1-8 and 14-19. Although pneumococci are still extremely sensitive to penicillin the drug becomes effective only up to a period of five days after the onset of pneumonia when most of the damage takes place. An effective polyvalent vaccine developed from the type specific polysaccharides of most of the harmful pneumococci would overcome this problem and we would move back from cure to prevention.

On the heels of the epidemic of Hong Kong type influenza which has swept with unexpected speed through most of our states, the National Institutes of Health, Institute of Allergy and Infectious Disease at Bethesda, Maryland has now launched a program aimed at preventing rather than wait to cure one of the main complications of influenza-pneumonia. A contract of $214,000 has been awarded Eli Lilly and Company to develop and make for experimental use two million doses of vaccine against the main Pathogenic types of pneumonia bacteria. This is the be backed up with $400,000 by a nationwide surveillance program involving 400,000 people and ten hospitals or health organizations in which the bacteria which should first be attacked and the types of people who should first be immunized, will be defined.

Testing of the vaccine on humans is expected to take place next autumn and a polyvalent vaccine for mass vaccination of high risk groups should be ready by 1970. If the vaccine comes up to expectation it could reduce deaths from pneumococcal pneumonia by 60 per cent and could save 50-100 million dollars in hospitalization and medical costs. The most desirable pneumonia vaccine would be one effective against pneumococci, pleuropneumonia like organisms and viruses. This would, of course, increase the volume of vaccine which would have to be injected and will also increase the reactivity of such a vaccine to the host. Problems of this kind however are technical and should not be too difficult to overcome.

By starting this project through subsidizing the pharmaceutical industry to produce a vaccine the Government has accepted responsibility for the health of our people. At the same time the pharmaceutical industry will mobilize its skill before waiting for assurance that their product will be assured of a profit. L.H.N.

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Technical Aspects of Surgical Management of a Right Hepatic Artery Aneurysm

Allan L. Toole, M.D., Harold Stern, M.D., Samuel Lerner, M.D. and Robert Lowman M.D.

A Case Report

A 47 year old male was admitted to the Yale-New Haven Medical Center in August 1969 with a known hepatic artery aneurysm. This had been discovered three months earlier while the patient was undergoing cholecystectomy for chronic cholecystitis with cholelithiasis. It had been decided not to repair the aneurysm during that procedure but to readmit the patient following convalescence for arteriography and definitive repair. The past history noted an appendectomy in 1943 and excision of an L5-S1 herniated lumbar disc in 1957. He had been well until six months prior to his cholecystectomy at which time he began to have postprandial distress following fatty food intake. Films at that time showed gallstones and duodenal ulcer. The latter healed, by x-ray, five months later but epigastric pain, radiating subcostally to the posterior midline bilaterally, persisted. These attacks were not postprandial but were decreased by refraining from fatty foods. There had been no sign of gastrointestinal bleeding or jaundice and he had not had a recent severe febrile illness.

Physical examination was unremarkable except for ill-defined tenderness to palpation in the right upper quadrant. There was no bruit. Blood pressure was 130/90. The SGOT was 170 but other liver function studies, including amylase and lipase, were normal.

At the time of cholecystectomy a thrill and pulsatile mass were noted medial to the common duct. Dissection revealed this to be a thin walled arterial aneurysm. Cholecystectomy was completed. The postoperative course was satisfactory and the patient was relieved of epigastric pain. Three months later he was readmitted. A celiac arteriogram (Fig. 1) demonstrated a fusiform aneurysm of the right hepatic artery. There was a smaller artery to the right hepatic lobe originating from the aneurysm also. The left hepatic and the gastroduodenal arteries originated just proximal to the aneurysm. Liver function studies, including SGOT, were within normal limits (Table 1).

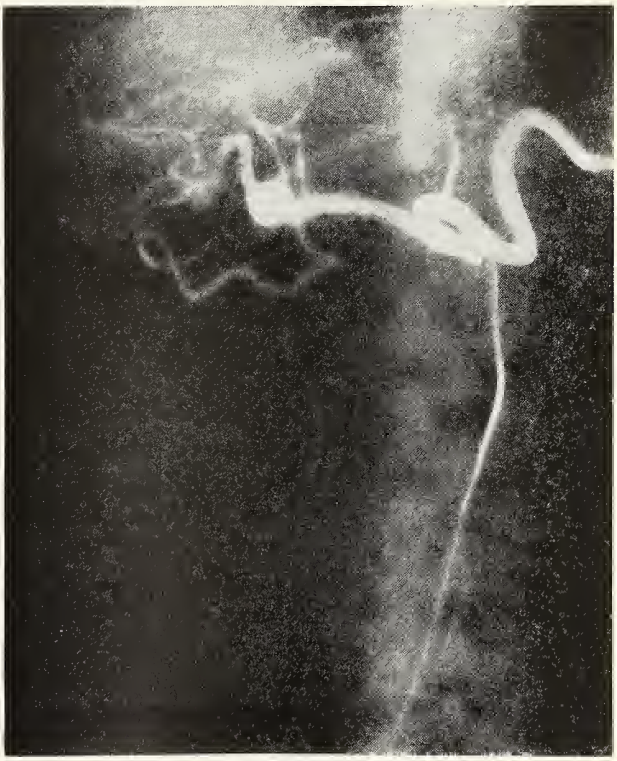

Figure 1

Preoperative celiac angiogram showing aneurysm of right hepatic artery.

The patient was premedicated with pentobarbital, 150 mg., morphine, 10 mg. and scopolamine, 0.5 mg. intramuscularly. Anesthesia was induced with thiopental, 250 mg. intravenously and maintained with nitrous oxide and oxygen 5 liter/2 liter flow rate. Succinycholine, 50 mg. was used to facilitate endotracheal intubation. A total of 45 mg. curare was given to prevent shivering and to provide muscular relaxation during the operation. A total of 20 mg. chlorpromazine was given intravenously for its anti-shivering and cryoprotective potential and 10 gm. of mannitol was given for its renal protective effect. 10,000 U. heparin intravenously was given prior to hepatic artery clamping and was reversed with 100 mg. protamine one hour later upon removing the clamps.

A hypothermia blanket and ice packs were used to cool to an esophageal temperature of 34°C before opening the old cholecystectomy incision. By the time the adhesions had been taken down, the aneurysm and its branches exposed, and a saphenous vein removed from the thigh, the temperature

TABLE 1

	Preop.	*Days Postop.* 2	4	8
Bilirubin	0.16/0.64	0.08/0.40	0.04/0.44	0.08/0.24
Ceph. floc.	0	0	0	0
Thymol turb.	2.8	0.5	0.7	1.5
Alk. phos.	56	31	43	46
Transaminase	28	62	46	35
LDH			360	290
Prothrombin time				10.5 sec.

DR. ALLAN L. TOOLE, Clinical Instructor Surgery; DR. HAROLD STERN, Clinical Associate Surgery; DR. SAMUEL LERNER, Clinical Instructor Anesthesiology; DR. ROBERT LOWMAN, Clinical Professor Radiology; From the Departments of Surgery, Anesthesiology and Radiology, Yale-New Haven Hospital, New Haven, Conn.

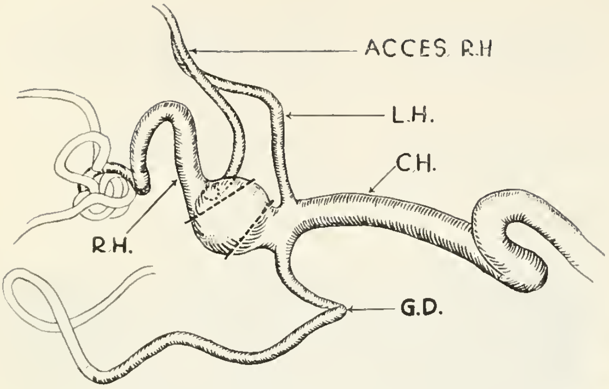

Figure 2
Drawing indicates site of excision.

had drifted down to 31.5°C. Two hours and 45 minutes had elapsed. The temperature remained stable at this level for more than one and one-half hours. After heparinization, one clamp was placed over the aneurysm distal to the origin of the left hepatic and gastroduodenal arteries, and a second one placed so as to occlude the main right hepatic artery and the smaller adjacent artery (Fig. 2). The aneurysm was excised in part and then the remaining portions were anastomosed with #6-0 polydek sutures incorporating the weakened vessel wall in the suture line (Fig. 3). The two vessels to the right lobe were occluded 24 minutes in order to complete the anastomosis. Reocclusion was necessary intermittently for an additional 26 minutes in order to secure hemostasis. The appearance of the liver remained unchanged throughout and there was a good pulse in both vessels at the completion of the anastomosis.

The hypothermia blanket was reversed to warming and the temperature rose to 34.1°C over the next two hours. 1 mg. atropine and 2.5 mg. of prostigmine were given to reverse the curarization and the patient was extubated. He was admitted to the recovery room awake and talking. Pathologic examination showed a typical arteriosclerotic aneurysm.

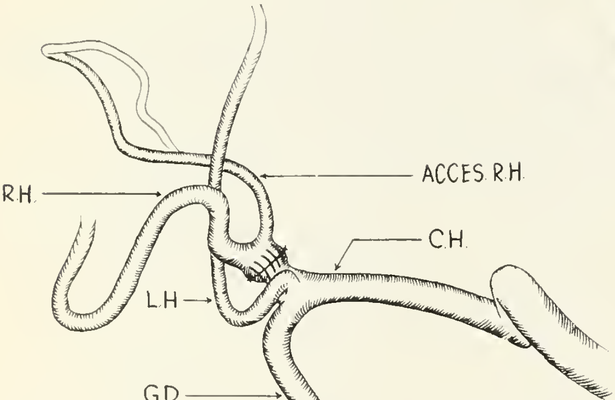

Figure 3
Drawing indicates primary repair.

Postoperatively, he developed phlebitis in the remaining long saphenous vein. This did not respond to Dextran and Heparin therapy was instituted on the sixth postoperative day. On the thirteenth day, while still heparinized, a repeat arteriogram was done (Fig. 4) which showed a patent anastomosis. Several hours following this, however, a femoral artery occlusion occurred and thrombectomy was necessary. He was discharged eight days later and remains in good health, now three months postoperative. Liver function studies (Table 1) showed only a transient rise in SGOT (normal 40) but otherwise remained normal.

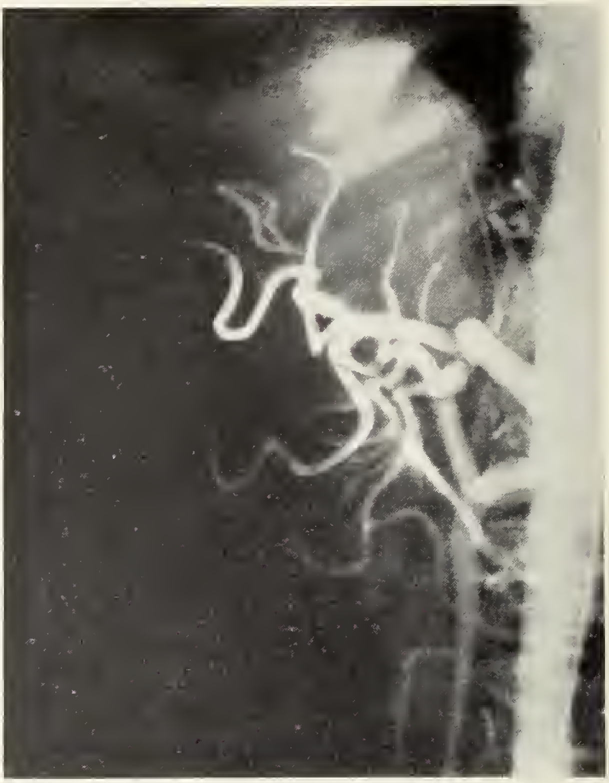

Figure 4
Postoperative angiogram showing repair with distal hepatic circulation intact.

Surgical Considerations

Previous reports have established the precarious prognosis for hepatic artery aneurysm. Guida and Moore[1] in a review article, report rupture of 103 of 165 reported cases in the literature at that time (1966). They added five cases of their own, three rupturing with resultant fatality. Despite the fact that information is not available on the percentage that do not rupture, it seems established that in a patient with a reasonable operative risk, surgery should be advised.

Arteriography[2] defines the vascular anatomy and dictates the operative approach. If the aneurysm is proximal to the gastroduodenal artery, it may be excluded by ligation without interrupting hepatic arterial flow because of adequate collateral flow. Aneurysms distal to this major collateral pathway pose a more complicated problem. Excision with bypass utilizing splenic artery, prosthetic[3] or vein graft, or direct repair (as in our case) may be indicated, depending on anatomical and technical factors.

Hepatic lobectomy may be necessary as a life saving measure if rupture has occurred. The use of ameroid constrictors in the experimental animal by Connolly[4] may have clinical application in the otherwise inoperable case with multiple or intrahepatic aneurysms. He has postulated that gradual occlusion of the hepatic artery causes adaptation of the liver to extract sufficient oxygen from the portal venous system.

Hypothermia seems particularly suited to the protection of the liver and its complex metabolism from anoxia. The additional occlusive time that moderate hypothermia (30°C-32°C) affords is not entirely clear but, as indicated by our case and others, as well as experience gained from liver transplantation, thirty minutes and probably as long as sixty minutes, appears to be safe.

It is interesting to speculate on the possible role of metabolic inhibitors, such as magnesium sulfate, in protecting the normothermic anoxic liver. From a practical standpoint, the two hours necessary for cooling and then for rewarming are the major deterrents to the use of moderate hypothermia. To our knowledge, magnesium sulfate has not been used clinically but it may have a role, particularly in the case in which emergency surgery is necessary to control intraperitoneal hemorrhage from rupture.

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TELECARE LAUNCHED IN WESTPORT-WESTON

The first meeting of the new Telecare Program committee of the Westport-Weston Chapter, American Red Cross, was held on June 8th, at the Chapter House. Attending were William Martin, retired executive of Chase Manhattan Bank, Chairman; Stephen B. Odell, retired executive of MONY in New York, Vice Chairman; Mrs. Donald Willard; Mrs. James Herndon; and Mrs. Rupert Foley.

The program is designed to serve elderly persons living alone in Westport and Weston through a free telephone check system. A group of volunteers is now being recruited to make regularly scheduled telephone calls to ascertain that all is well, and to send help in case of accident or illness. A letter is going out to local doctors, Churches, the Temple, Golden Age Club, and others, requesting assistance in compiling the list of persons living alone who wish to be phoned. All information is, of course, confidential.

Persons in Westport and Weston interested in being a part of this needed service to the communities, either as a person to benefit from the program, or as a volunteer to make calls, or for additional information about Telecare Program should phone American Red Cross, 227-2675 or 227-5333.

Management of Complications of Pancreatic Pseudocysts

J. Vilinskas, M.D.

Abstract

A presentation of the complications of pancreatic pseudocysts is made and their treatment discussed. It is stressed that these complications are much more frequent and more lethal than was previously recognized. A plea for early surgery of uncomplicated pancreatic pseudocysts is made.

Complications of pancreatic pseudocysts were once thought to be extremely rare. It is becoming obvious, however, that they occur in much greater numbers than previously suspected and that their treatment often constitutes a challenge in management. The most frequently encountered complications, and the most life threatening, are perforation and hemorrhage. Infection, ascites, compression of adjacent structures and unusual fistulous communications also occur, but these are of lesser clinical significance.

Much controversy and doubt still exist as to the best treatment of uncomplicated pseudocysts of the pancreas. The management of its complications is even less clearly defined.

It is the purpose of this paper to clarify some of these problems and establish guidelines in dealing with such complications.

Hemorrhage

In 1967 Cogbill[1] reported a total of only 16 cases of documented hemorrhage in pancreatic pseudocysts. Since then, several large series[2,3] of pancreatic pseudocysts have established that hemorrhage is much more common than was previously thought. Thomford and Jesseph reported fifty cases of pseudocyst, ten of which (or 20%) developed hemorrhage from the cyst.

The bleeding may be into the cyst, the free peritoneal cavity, or into an adjacent viscus such as the stomach, duodenum, or colon. It is usually due to the erosion of the splenic, superior mesenteric, or gastroduodenal arteries, although any vessel in the path of the encroaching pseudocyst may be involved. The hemorrhage is characteristically severe and carries a high mortality rate.[2] It may present as a gastrointestinal hemorrhage, since the hemorrhage frequently accompanies spontaneous fistulization of the cyst into an adjacent loop of bowel or stomach; it may present as a free intraperitoneal hemorrhage resulting from a concomittant free perforation of the cyst or erosion of one of the vessels adjacent to the cyst; lastly, it may be intracystic, where the only signs are pain accompanied by an enlarging abdominal mass, which may be pulsatile.[4] The hemorrhage can occur as the first manifestation of the cyst, while the patient is under medical management, or it may follow surgical treatment designed to drain the cystic cavity.

Clinical diagnosis depends on demonstration of gastrointestinal bleeding or a dropping hematocrit in a patient who is a likely candidate for the development of a pseudocyst. Since the majority of cysts follow pancreatitis or pancreatic trauma, these patients become especially suspect if clinical evidence of bleeding occurs. Most of the patients give a history of nausea, vomiting, and weight loss, and physical examination may or may not reveal an abdominal mass and tenderness. Besides a dropping hematocrit, there will be some leukocytosis, and about half of the patients will show an elevated serum amylase level. The most helpful diagnostic study is the barium meal which will show displacement of the stomach, colon, or duodenum by a mass in 70 to 85%. Although diagnosis is seldom made prior to exploratory surgery or autopsy, evidence of bleeding, especially if severe, in a patient with suspected pancreatic pseudocyst should always alert the physician to the possibility of a hemorrhaging pseudocyst.

We recently had an opportunity to attend a fifty-eight year old chronic alcoholic with advanced cirrhosis of the liver, who presented with an exsanguinating upper gastro-intestinal hemorrhage. Emergency esophagogastroscopy revealed a 3 × 3 cm. ulcer crater on the posterior wall of the stomach with active arterial bleeding. At the time of surgery the described "ulcer" was found to be the mouth of a large pancreatic pseudocyst in the tail of the pancreas which had spontaneously drained into the

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stomach. There was active hemorrhage from the walls of the cyst and from the junction of the cyst and stomach. Because the cyst involved the spleen and the splenic flexure of the colon, a distal pancreatectomy was not done. The mouth of the cyst was oversewn with a running locked stitch of 00 chromic catgut and the cyst was packed with iodoform gauze. On the fourth post-operative day, the pack was removed on the ward through the gastrostomy incision with no evidence of rebleeding.

Since many of the patients with hemorrhagic pseudocysts have concomittant liver disease and are usually poor surgical risks, the tendency is to treat such patients medically with repeated blood transfusions or to subject them to as little surgery as possible at the time of initial exploration. Definitive surgery is planned at a later date but all too often there is rapid deterioration and death with continued or recurrent hemorrhage.

From our own experience and that of others we feel the management of this complication is twofold; prevention and aggressive surgical attack. The tendency in the past, among the internists as well as the surgeons, has been to wait in the hope that the pseudocyst will regress spontaneously. The cyst may regress or disappear clinically, only to reappear again in a matter of days or weeks. In a few cases where a pancreatic mass is palpable and demonstrable on X-rays operation discloses only an edematous gland with a closely adherent omentum, which is mistaken for a cyst. Spontaneous healing of the cyst has been reported but is probably rare.

The custom of allowing pseudocysts to "mature" for several weeks so as to allow a thick fibrous wall to form which will hold suture material more securely is commonly practiced by surgeons. It has become apparent, however, that often these patients encounter fatal complications in the form of hemorrhage or perforation while being observed. Thomford and Jesseph[2] have reported six patients in their series of fifty who developed fatal complications while awaiting surgery.

We feel it is wisest to operate as soon as the diagnosis of pseudocyst is made. A variety of surgical procedures can be employed depending on size, location, and character of the pseudocyst.

In dealing with the acute hemorrhage, management has to be aggressive. Surgical intervention is almost always necessary to control such bleeding. Temporizing procedures such as packing of the cyst should be reserved for the poorest surgical risk patients and where the inflammatory mass is so extensive as to make resection prohibitive. Packing of the cyst has proved to be inadequate and there is a great tendency to rebleed after its removal or go on to develop intra-abdominal abscesses and septicemia.

The operation of choice is one which controls the bleeding and drains the cyst. If an active point of bleeding can be found, ligation with a drainage procedure is best. The anastomotic line should be oversewn with a hemostatic lock-stitch of 2-0 chromic catgut to prevent post-operative hemorrhage. Where the source cannot be identified or if the source is a generalized oozing from the wall of the cyst, the treatment becomes more complicated and resection of the cyst with a portion of pancreas (particularly suitable for lesions of the tail of the pancreas) is indicated. Duodenopancreatectomy is indicated in lesions which are not amenable to the above measures, and where the inflammatory response is not so extensive as to make resection of involved structures quite hazardous.

The surgeon must judge at the time of exploration which of the above procedures suits the particular occasion and which offers the patient the greatest chance of survival. Every effort must be made, however, to do definitive rather than a temporizing procedure at the initial operation, since deterioration of these patients is rapid with successive complications and repeated hemorrhages.

Perforation

In 1960 Hanna[5] reported the incidence of spontaneous perforation of pseudocysts to be 5%, although more recent studies suggest it may be as high as 20%.[2,3]

Perforation may occur into the general peritoneal cavity, where it presents as an acute surgical abdomen with shock, or it may perforate into adjoining organs such as the stomach, colon, or intestine. Most commonly, perforation is accompanied by some degree of hemorrhage, but cases of entirely asymptomatic spontaneous drainage into the gastrointestinal tract are not common.

Perforation of the pseudocyst commonly occurs in the early stages of the cyst formation before a thick fibrous wall forms. Therefore, the common practice of allowing pseudocysts to mature before surgery is undertaken often leaves the patient vulnerable.

Where free perforation into the peritoneal cavity occurs, there is clinical evidence of rapidly developing shock and the characteristic signs of an acute abdomen. Leukocytosis and serum amylase elevation are commonly present. Characteristically, a palpable abdominal mass will suddenly disappear in the face of rapidly increasing abdominal signs and shock. Emergency surgery is imperative. The cyst must be drained and the abdominal cavity cleared of all necrotic material and pancreatic juices.

Where only perforation has occurred the surgical treatment is simple and effective. The cyst is drained, either externally or into the intestinal tract, so as to prevent further peritoneal contamination. Complete recovery is the usual course. If hemorrhage is an accompanying factor, treatment is more difficult and results poorer. The effectiveness in dealing with the accompanying hemorrhage often determines the patient's course.

We have recently treated two patients whose pseudocysts ruptured while under medical management. One of these patients who had a simple free perforation underwent an emergency cystgastrostomy and had an unremarkable recovery. The second had concomittant hemorrhage from the cyst wall which was treated by packing and external drainage. He rebled following the removal of the pack, and although a subsequent procedure controlled this hemorrhage, he went on to develop multiple abdominal abscesses and eventually died from uncontrolled septicemia.

Where perforation occurs into an adjacent viscus such as the stomach, colon, or small bowel, no further treatment is necessary if there is no accompanying hemorrhage. Furthermore, these internal fistulas may be asymptomatic and may account for some of the spontaneous "cures" of the pseudocyst.

Infection

A pancreatic abscess is always preceded by pancreatitis and is said to develop in about 3% of all cases of acute pancreatitis.[6] They are especially apt to develop in hemorrhagic pancreatitis where necrotic pancreatic tissue admixed with blood forms an ideal culture media. It is hard to say how many such pancreatic infections start out as pseudocysts which become secondarily infected. The contents of a pseudocyst are usually sterile and made up by a clear or slightly turbid fluid, but up to 20% of cultured pseudocysts show the presence of microorganisms.[2] Since the contents of a pseudocyst are not ordinarily conducive to the multiplication and growth of organisms, some change in the intracystic environment (perhaps a hemorrhage) is necessary before bacteria can flourish. The diagnosis and treatment of such an infection is essentially that of a pancreatic abscess.

The single most important clue to the existance of a pancreatic infection is the sudden development of fever in a patient with subsiding pancreatitis or following pancreatic trauma where no other obvious source of infection is apparent. These patients will complain of some abdominal pain and tenderness. Frequently chronic malaise, fever, anorexia, and weight loss a month or longer after the acute episode are the only indications of a smoldering infectious process. Leukocytosis, anemia, and persistently elevated serum amylase are common, although not always present. X-rays frequently show a left pleural effusion, and may show typical small gas bubbles in the area of the pancreas. Most characteristically there will be only widening of the duodenal loop or displacement of the stomach and colon on barium examination.

An infected pseudocyst, which has well defined fibrous walls, may be evacuated and drained much the same way as an uncomplicated cyst. If, on exploration, the infected pancreas is poorly defined with a friable inflammatory wall it is best to evacuate the necrotic material and the area is drained with a large sump catheter and several soft rubber drains. The pancreatic area seals off from the rest of the abdominal cavity rather rapidly and in 3-5 days irrigations with saline can be started to remove all residual necrotic material.

Once a pancreatic abcess forms, the mortality rate is close to 100% if left untreated, and about 40% when drained.[6] The morbidity rate following surgical drainage is high and a complicated postoperative convalescence is usual. Appropriate parenteral antibiotics based on sensitivity of the cultured organism is always employed. Since pancreatic infections don't have a predilection for any one specific organism, broad spectrum coverage is indicated until antibiotic sensitivities are available. A variety of organisms can be culture with E. coli and Staph aureus predominating.

It is interesting to note that the incidence of pancreatic abscess has dropped from nine to three percent since the common practice of using antibiotics to treat acute pancreatitis.

Ascites

Recently, the so-called "pancreatic ascites" has been recognized and described.[3] It is characterized by the presence of an amylase-rich ascitic fluid which occurs in association with pancreatic pseudocysts or, more rarely, with pancreatitis, when no other cause of ascites can be found. It is estimated to occur in 13% of all pseudocysts. Its pathophysiology is thought to be a disrupted pancreatic duct or a slowly leaking pseudocyst. In this entity, the ascitic fluid is high in amylase and the protein level is 3 gms. or higher, where ascites of cirrhotic origin has little or no amylase activity and the protein level is below 3 gms.[7]

Surgical drainage of the cyst is indicated and is usually curative. Rosenberg,[3] however, reported that three of his seven cases of pancreatic ascites treated surgically recurred, and half of the patients with a recurrent pseudocyst previously had ascites. Undoubtedly, the continued use of alcohol with recurrent pancreatitis and new pseudocyst formation may have contributed to the poor results. When the etiology of the pseudocyst is unrelated to the continued use of alcohol, satisfactory and permanent cure can be expected.

Other Complications

Since a pseudocyst may form in a variety of intraabdominal locations presenting symptoms may be unusual and bizarre. A pseudocyst in the head of the pancreas may present as obstructive jaundice because of impingement of the large cyst on the ampulla or the common duct and it may be clinically indistinguishable from carcinoma of the head of the pancreas. A cyst may obstruct the duodenum partially or completely. The pseudocyst may compress other adjacent structures such as the inferior vena cava and the patient will present with unexplained edema of the lower extremities, or it may compress the portal vein and precipitate portal hypertension and hypersplenism.

Left and right sided hydrothorax has been described in association with a pseudocyst and the pleural fluid characteristically has a high amylase level. This syndrome is thought to be due to a direct leak of the contents of the pseudocyst into the pleural cavity or a transudation of the pancreatic fluid through the diaphragm.

Although diabetes mellitus is reported in 45 to 75% of cases of pseudocyst, this probably represents the underlying pancreatic disease and is not directly due to the pseudocyst itself.

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DRUG EDUCATION

The Society office has available a collection of publications which discuss drug abuse and drug dependence. Physicians wishing to receive sample copies of the following pamphlets should contact Leonard R. Tomat, Assistant Executive Director for Educational and Scientific Activities, 160 St. Ronan Street, New Haven, Connecticut, 06511:

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Surgical Correction of Congenital Coronary Defects

I. Anomalous Origin of the Left Coronary Artery from the Pulmonary Artery

John A. Ogden, M.D.

Anomalous origin of the left coronary artery from the main pulmonary artery is an infrequent lesion that many clinicians arbitrarily divide into infantile and adult patterns. However, these two phases represent the extremes of a syndrome that may manifest through a diversity of signs and symptoms: angina in a three month old, mitral insufficiency in a seven year old, sudden death in a twenty year old, or an asymptomatic continuous murmur in a forty-year old patient.

Because only a small percentage survive the early phases of the syndrome, and because those who survive still face the problems of continued symptoms (primarily exertional angina) and the threat of sudden death, this lesion should be corrected surgically. To date, 94 patients, including 15 in the current series, have undergone various surgical procedures, with 61 survivors.[1] Followup in most reported cases has been brief. This paper will present an analysis of the various operative procedures and results, and will include several long-term followups from the current series.

Case Material

The current series, the largest yet reported, includes 39 cases representing all phases of the clinical syndrome. Interestingly, none were greater than twenty years of age. There were 24 females and 15 males. Fifteen patients underwent surgery and are summarized in Table 1.. Two of the cases are quite unusual. In case 7 an initial attempt to ligate the origin of the left coronary artery resulted in severe ischemic changes and permanent ligation was not done. Four years later the adhesions from the previous surgery precluded external ligation and the patient was placed on cardiopulmonary bypass. A pulmonary arteriotomy was performed and the ostium of the left coronary artery was oversewn without difficulty. The patient is asymptomatic three years later. Case 14 was initially thought to have congenital mitral stenosis and underwent prosthetic replacement of the mitral valve at the age of two years. She did well for a year, but during the ensuing year developed signs of recurrent mitral stenosis. Surgery revealed the first prosthetic valve was covered by a thick fibrous layer, and a second valve was inserted. The patient died two days later, and autopsy revealed the anomalous left coronary artery.

Ten cases underwent ligation of the left coronary artery. Seven are doing well three to eight years after the procedure. However, electrocardiographic evidence of exertional ischemia persists in two patients, both of whom underwent surgery relatively late (cases 4, 7). The three deaths occurred in patients operated on during the first year of life. In four other cases the preoperative diagnosis was congenital mitral disease, and the surgery was directed only at the mitral valve. All four died, and autopsy revealed the anomalous left artery in each case. One patient underwent pericardial poudrage, and shows no evidence of constrictive pericarditis two years after surgery.

Discussion

Classification is an empirical device that often needs revision. The initial reports of two apparently distinct groups led to the term' infantile' and 'adult.' Later the terms 'transition phase' and 'coronary steal' were added. But this congenital lesion must be conceived of as a dynamic lesion, not a series of discrete phases. Further, most deaths occur within the first year of life, and those patients surviving beyond the first year have all the features of the 'adult' phase, except chronological age. Therefore, it is proposed that the terms 'infantile' and 'adult' be replaced, respectively, by the terms 'immature' and 'mature.' The concept of transition phase should be retained, as this describes the period of collateral development between the immature and mature phases. The 'coronary steal' should be deleted, as this is an integral part of the mature phase, and probably exists to a lesser degree in the immature phase once pressure in the pulmonary artery drops to extrauterine levels. The size of the 'steal' varies in each patient, just as the shunt varies in patients with coronary artery-cardiac chamber fistulas. This allows a more accurate description based upon the pathophysiology of the lesion—the

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TABLE 1

SUMMARY OF FIFTEEN OPERATED CASES

Case	*Sex*	*Symptom Onset*	*Operation*		*Results*
			Age	*Procedure*	
1	F	4 mo	6 mo	Ligation	Postoperative angina and death
2	F	4 mo	4 mo	Ligation	Angina for two months; asymptomatic after 6 years
3	F	7 mo	22 mo	Plication of mitral valve	Postoperative death
4	F	7 mo	16 yr	Ligation	ECG changes remain 4 yr later
5	M	4 mo	9 yr	Ligation	Residual MI 5 yr later
6	F	3 mo	5 yr	Poudrage	Good 2 yr later
7	F	5 mo	a) 16 yr	Unsuccess ligation	Continuing exertional angina
			b) 20 yr	Ligation (arteriotomy)	Asymptomatic 3 yr later
8	M	7 yr	8 yr	Mitral prosthesis	Postoperative death
9	M	3 mo	3 mo	Ligation	Postoperative death
10	F	1 mo	16 mo	Ligation	Postoperative death (8 d)
11	M	3 mo	8 yr	Mitral prosthesis	Postoperative death (5 d)
12	F	7 yr	8 yr	Ligation	Asymptomatic 8 yr later
13	M	4 mo	a) 6 mo	Explor Thoracotomy	Exertional angina
			b) 6 yr	Ligation	Asymptomatic 6 yr later
14	F	3 mo	a) 2 yr	Mitral prosthesis	Recurrence of MS
			b) 4 yr	Mitral prosthesis	Postoperative death (2 d)
15	F	6 yr	6 yr	Ligation	Asymptomatic 8 yr later

development of functioning collateral circulation between the right and left coronary arteries.

One of the first proposed operations was aortopulmonary anastomosis. The purpose was to raise pressure and oxygen saturation in the proximal pulmonary artery and, thereby, the left coronary artery. Three attempts were unsuccessful, with two patients dying during surgery, and one a few hours after surgery. A serious disadvantage of the procedure was the increased workload on an already failing left ventricle.

Supravalvular banding of the main pulmonary artery was also attempted, the reasoning being that the sustained pressure increase would enhance the effective flow to the left coronary artery, despite the lessened oxygen saturation. One attempt was unsuccessful.

Several methods were proposed to increase the development of collateral circulation from sources other than the coronary arteries. These included pericardial poudrage, chemical deepicardialization and cardiopneumopexy. Fifteen patients underwent one or more of these procedures. Five patients also underwent concomitant ligation of the left coronary artery. Two patients died shortly after surgery and a third died three months later. One patient developed a severe constrictive pericarditis. The other eleven patients are doing well a few months to eight years after surgery.

Ligation of the left coronary artery at its origin from the pulmonary artery was attempted following the revival of the concept that flow was from the right coronary artery to the left coronary artery to the pulmonary artery. The objective of the procedure is to redirect the higher pressure flow from the right coronary artery and close the left-to-right shunt into the pulmonary artery. Provided there are sufficient intercoronary anastomoses, ligation causes increased perfusion pressure within the left coronary artery, as well as an increase in oxygen saturation. Therefore, operative success is contingent upon the development of collateral circulation. If the communications are sparse, as in the immature and early transition phases, ligation can lead to ischemia and death. In contrast, the adequate collateral circulation of the late transition and mature phases enhances success.

To date 59 patients have undergone ligation of the left coronary artery (Table 2). 28 were less than eighteen months of age. Of these, fourteen survived and were clinically improved, although the electrocardiographic changes persisted in many. These patients were operated on as early as five weeks of age. Most deaths occurred in the immediate post-

TABLE 2

OPERATIVE RESULTS

Age at operation/procedure	*Cases*	*Survivors*	*Survival*
< 18 mo./all procedures	49	25	51%
< 18 mo./ligation only	28	14	50%
> 18 mo./all procedures	42	33	79%
> 18 mo./ligation only	31	30	97%
> 18 mo./anastomosis only	6	6	100%

operative period. One of the postoperative deaths lived eleven months.

Thirty-one cases greater than eighteen months of age underwent ligation. There was only one postoperative death—that being an eight year old who had a mitral annuloplasty during the same operation. Again, while most improved, electrocardiographic changes persisted in many.

Three of the patients who underwent ligation of the left artery were corrected by oversewing the ostium from within the pulmonary artery. All three were doing well postoperatively.

A disadvantage of ligation is the production of a single coronary artery. One case has been reported in which a patient died suddenly three months after ligation, and autopsy revealed a fresh, occlusive thrombus in the proximal right coronary artery.

To obviate such a rare complication, the preferrable method would be anastomosis of the left coronary artery to the aorta, or to another systemic artery. Several attempts were made to anastomose to the left carotid, left subclavian, or aorta. All were unsuccessful until recently. Cooley[2], in five patients, and Reis[3], in one patient, have used autogenous vein or dacron grafts to anastomose the left coronary artery to the aorta. All six are doing well.

Summary

If the patient is less than eighteen months of age, the probability of sudden death is high, and the morbidity and mortality of surgery are increased. Undoubtedly, the procedure of choice would be anastomosis, thereby obviating dependence upon the development of collateral circulation. However, such a procedure is technically difficult in the infant.

The results in patients greater than eighteen months of age are much more gratifying, with an overall survival of 80%, and an even higher survival if one considers only ligation and anastomosis.

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KIDNEY FOUNDATION DRUG BANK

The Kidney Foundation maintains a drug bank for patients with renal disease. Providing drugs at the lowest possible costs to a patient is the objective of this service to Connecticut residents through Foundation headquarters at 357 Whitney Avenue in New Haven.

A patient may benefit from this drug bank once his physician sends in a completed registration form and a prescription. A complete list of available drugs is available from either the CSMS office or the Foundation headquarters. All medication will be handled by mail, thus making the service readily available to the physician and/or the patient.

Acute Arthritis of the Sternoclavicular Joint Due To Coliform Bacillus

Allen F. Delevett, M.D. and David T. Monahan, M.D.

Synopsis Abstract

An acute monoarticular arthritis of the sternoclavicular joint due to Coliform Bacillus, only the second reported in the literature, is presented. The occurrence following an acute gastroenteritis, the value of tomograms in the diagnosis, and the etiological diagnosis and treatment by surgery are discussed.

The authors have found only 18 cases of monoarticular arthritis of the sternoclavicular joint reported in the literature[1] and only one previous report of this disease due to infection with Escherichia coli,[2] in spite of the known increase in incidence of septicemia due to coliform organisms.[3]

Report of a Case

A fifty-seven year old white female was admitted for severe pain in the right upper chest of 10 days' duration. Two weeks prior to admission she had experienced nausea and vomiting for one week. Four days after these had subsided, pain appeared in the right trapezius area and right upper arm, accentuated by motion of the shoulder. Within a few days, a tender swelling appeared in the region of the right sternoclavicular joint. Physical examination on admission showed a well-developed, well-nourished, white female in severe pain, aggravated by the slightest motion of the arm and with an oral temperature of 100.8 F. Positive physical findings were confined to the right upper anterior chest and right supraclavicular area where there was an erythematous, exquisitely tender, hot, markedly swollen area measuring 10 by 13 centimeters. Maximum tenderness was present over the region of the sternoclavicular joint where the skin showed considerable dimpling. White blood count on admission was 20,000/cu.mm. with 75% segmented neutrophils and 2% band forms. Hemoglobin was 11.2 grams/100 ml. and hematocrit reading was 35.5%. Urinalysis showed 100 white blood cells per high-powered field and trichomonas vaginalis. VDRL test, blood culture on admission, and serum agglutinins for typhoid, paratyphoid, brucella, and proteus X-19 organisms were negative. Conventional p.a. and lateral films of the chest as well as a special lateral view with hyperadduction of the shoulders revealed only soft tissue density of the right upper anterior chest wall. Tomographic films of the upper sternum and right sternoclavicular area showed a definite destructive process in the medial end of the clavicle with destruction of the articular surface of the sternoclavicular joint and some degree of destruction of the adjacent manubrium. The diagnosis of septic arthritis of the sternoclavicular joint seemed evident. Aspiration of the joint for culture was not performed for two reasons—first, the outlines of the joint were completely obliterated by the marked inflammatory edema of the upper chest and supraclavicular area and second, blind aspiration seemed dangerous in this area. A urine culture taken on the second day of hospitalization was negative as were ten additional blood cultures. On a regime of Penicillin and Streptomycin for the first 24 hours and of Methicillin 4 grams a day from the second through the eleventh day, the acute signs and symptoms and leukocytosis gradually subsided. On the twelfth day, there was an abrupt recrudescence of fever to 105.0°, associated with shaking chills. On the morning of the 13th day, a 5-inch incision was made over the right clavicle extending from the region of the sternoclavicular joint. The underlying muscles and the tissues of the joint were thickened, edematous and hemor-

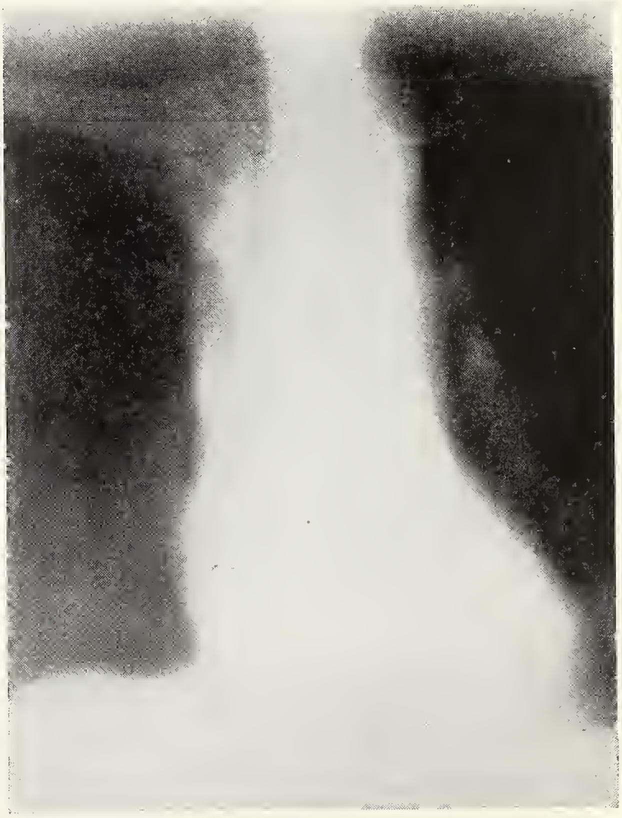

Figure 1
Tomogram at 4.5 cms., showing destruction of the right sternoclavicular joint and adjacent bone.

DR. ALLEN F. DELEVETT, Senior attending physician, chief of section of Internal Medicine, Senior attending cardiologist, Bridgeport Hospital, Bridgeport, Conn.

DR. DAVID T. MONAHAN, Senior attending surgeon, Bridgeport Hospital, Bridgeport, Conn.

rhagic. The joint was felt to be fluctuant but no pus was obtained on aspiration or on opening. The first costochondral junction seemed to be separated from the first rib. The medial three inches of the clavicle, the sternoclavicular joint, the distal end of the first rib, and the first costochondral junction were all removed. Cultures taken during the operation from tissues outside the sternoclavicular joint as well as within the joint and from the specimen of the first rib after being received in the Surgical Pathology Laboratory were all positive for Escherichia Coli and Coliform Bacilli. Sensitivity testing by the disc method showed these organisms to be sensitive to Ampicillin, Cephalothin, Chloramphenicol, Tetracycline, Streptomycin, Polymyxin B, Colymycin and resistant to Methicillin, Oxacillin, Cloxacillin, Lincomycin and Novobiacin. Postoperatively from the 15th through the 22nd hospital day, the patient received Dihydrostreptomycin 0.5 gram every 12 hours i.m. She made an uneventful recovery and has remained well to the present date. Prior to discharge, intravenous pyelograms, Barium enema and gall bladder series were done and were normal. Pathological report on the resected tissues was non-specific acute and chronic inflammation of the sternoclavicular joint and sternal margin of the clavicle.

Comment

Since no source of acute or chronic localized infection, that could have resulted in bacteremia and resultant spread to the sternoclavicular joint, was found in the urinary tract, colon or gall bladder, it is interesting to speculate further on possible site of blood stream invasion. The gastroenteritis preceding the onset of joint manifestations could conceivably have been accompanied by an invasion of the blood stream by coliform organisms and this is further suggested by the appearance of joint symptoms four days after subsidence of nausea and vomiting. However, in septic arthritis, failure to find a portal of entry is common.[4] None of the other factors described in the etiology of septic arthritis were present—namely, trauma, rheumatoid arthritis, presence of other debilitating disease or intra-articular injection of adrenal steroids. It is probable that she had pre-existing asymptomatic osteoarthritis of the sternoclavicular joint since Sokoloff and Gleason[5] have shown that after the fifth decade this joint rarely shows absence of degenerative changes.

The diagnostic, therapeutic and prognostic importance of joint aspiration in septic arthritis has been stressed[6] but this procedure was not done because the loss of all identifying landmarks made aspiration a blind and dangerous procedure. Our operative bacterial sensitivity studies did not correlate with the definite clinical impression of early response to Methicillin administration but were bolstered by failure to eradicate the infection prior to surgery.

The value of tomograms in demonstrating osseous and articular lesions that are not visible on standard roentgenograms has been stressed[7] and was again demonstrated in this case.

Methicillin—Staphcillin
Erythromycin—Erythrocin

Reprint request to Dr. Allen F. Delevett, 114 State Street, Bridgeport, Connecticut.

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(1) Septic arthritis
(2) Sternoclavicular joint
(3) Coliform Bacillus

THE PRESIDENT'S PAGE

The planners, both professional and amateur, are continuing their efforts to change the medical care delivery system. This could be healthy since no system is perfect and we all know that changes must be made in the present system if we are to continue to provide high quality medical care to an increasing population which is rightfully demanding more and better service. However the planners must be objective and not plan just for the sake of planning. Unfortunately this is not always the case.

Good planning requires a prior thorough study of the problems and careful objective evaluation of the various possible methods of solving them. The older professional planners are bogged down in their previously conceived solutions to the problems while the younger professionals and the amateurs are not thinking for themselves but following the lead of the "old pros". Thus we find ourselves in the position that the remedies of the 1950's are being recommended and even implemented to solve the problems of the 1970's. Too much has happened on the medical care scene since 1950 for us to blindly accept the solutions of the 1950's and expect them to solve the problems of the 1970's.

The policy statement recently adopted by the Council of the Connecticut State Medical Society states in part: "Any plan or plans for delivery of medical care which best suit the needs of any given locality are acceptable." This should be one of the prime considerations in implementing any plan—that it best suit the needs of the people.

Since 1950 there has been a growing shortage of physicians not overcome by the increase in the number of physicians graduated. It also remains to be seen what impact the use of paraprofessionals and doctor's assistants will have on the physician shortage. Any new system for delivery of medical care must cope with this problem.

Another factor in medical care is the cost of hospital and clinic care. Hospital costs have risen dramatically since 1950 and at present, hospital clinic charges, calculated on a "cost" basis, are between double and triple those of private practitioners in the same community. This would indicate that the hospital setting is not an economic location to provide ambulatory care. Information from the Hill Health Center, a federally funded program in New Haven, also indicates a high cost of operation. Its director is quoted in *The New Haven Journal-Courier* (Aug. 6, 1970) as stating that it costs $15.00 "everytime someone walks in the door". It would appear that highly organized large-scale facilities for delivering medical care have a high overhead. What then should be the optimum size of a facility taking into consideration the provision of high quality care at reasonable cost?

The concept of the multi-specialty groups as the ideal method of delivering medical care is one that has been sold to the American public for many years. This has been accepted by the people in the federal government so that it has been included as Part C (Health Maintenance Organizations-HMO) in the proposed new Medicare regulations. When I visited the Department of Health, Education and Welfare in Washington recently I asked for information on this subject. I was interested to know whether any recent studies had been made of this type of medical practice particularly from the view-point of cost, quality and physician efficiency (number of patients seen per physician per hour or work day). The latter is becoming increasingly important in the light of the physicion shortage. The people I spoke with in Washington did not know the answer. It is important however that we do know what such a system can now provide, at what cost, at what level of quality and efficiency. In order to obtain this information it may become necessary for physicians through their own organizations to perform the study.

The policy statement of the Council also states in part: "Forcing one delivery system on a state or community wide basis through propaganda or financial subsidy is short-sighted, and not in the best interest of the public to be served". Unfortunately this does occur, without knowledge and even in disregard of its impact on other segments of the community.

The Regional Medical Programs were created to improve the care of patients suffering from Heart Disease, Cancer and Stroke. In Connecticut the program has chosen to enlarge its scope beyond the three disease categories. In doing so it has funded a "Third Faculty" for the medical schools in the form of full-time Chiefs of Services in Community Hospitals. While one cannot take issue with a program on philosophic grounds, is this a proper use of medical manpower in a time of increasing shortage? Also what impact will this have on hospital rates when the physician's salary will later be paid in full by the hospital? Our AMA President has told us that there are already too many physicians in fulltime positions and that hospital education programs presently cost the patient $5.00 per day. Will this add another dollar or two per day to the patient's bill?

Another question which needs answering is whether the full-time Chiefs of Services are to provide the cadre for future multi-specialty groups based in the hospitals, expensive sites for ambulatory care. If so this might be a form of financial subsidy which the Council disapproves.

Furthermore is this program in tune with the times or is it one that was conceived to solve the problems of ten years ago. The needs of the people in the 1970's will be such that changes will have to be made in our medical care delivery system. Just what those changes should be requires careful and thorough study. It may be necessary to experiment with different plans in various places as pilot programs and perhaps change them as we go. However we must be open-minded and objective and be ready to discard what doesn't work and try something else. We must continually bear in mind what is best for our patients. It is up to us to find a way to provide this within the framework of our present political and economic structure. We must not be influenced by the propaganda for the remedies of the 1950's unless we are convinced they will solve the problems of the 1970's.

Morris A. Granoff, M.D.

FROM THE EXECUTIVE DIRECTOR'S OFFICE

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Associate Executive Director

Leonard R. Tomat
Assistant Executive Director
Scientific Activities

SUMMARY OF ACTIONS COUNCIL MEETING
Wednesday, July 15, 1970

I. Attendance

Present in addition to the Chairman Dr. S. J. Martin, and the Vice Chairman Dr. K. F. Brandon, were: Drs. Granoff, Weber, Jr., Grendon, Burnham, Edson, Abbot, Dean, Gardner, Fabro, Rem, Cramer, Harwood, Pelz, Roch, Nemoitin, Van Syckle, Freidberg, Johnson, Ragland, Jr., Freedman, Root, Jr., and vonGlahn.

Also present were: Mr. Sullivan, Mr. Tomat, Mr. Olson (FCMA), and Mrs. Lindquist.

Absent were: Drs. McDonald, Wilson, Jr., Palomba, Gorin, Purnell, and Klare.

II. Routine Business

Approval of Minutes

As printed and distributed, it was VOTED to approve the minutes of the meeting of June 4, 1970.

Life Memberships

It was VOTED to approve applications for Life Membership received from the following eligible Active Members:

Robert H. Abrahamson, High Valley Way, Stamford (FCMA)—1970
Charles E. Dyer, 297 Montauk Avenue, New London (NLCMA)—1970
Willard J. Morse, East Braintree, RFD #2, Randolph, Vermont (NLCMA)—1970
Michael W. Palmieri, 690 Howard Avenue, New Haven (NHCMA)—1/1/71
Robert L. Pollard, Birchwood Ter., Prospect (NHCMA)—1970
Nathan Weinstein, 3 Club Mountain Road, Norwalk (FCMA)—1/1/71

Resignations, Appointments, etc.

Committee on Hospitals: It was VOTED to accept, with regret, the resignation of George E. Roch, Willimantic, as a member of the Committee. It was further VOTED to appoint Frank L. Bird, Willimantic, to the Committee.

Committee on Allied Medical Service: It was VOTED to accept, with regret, the resignation of William A. Whalen, Willimantic, as a member of the Committee.

Ad Hoc Committee to Study Hospital Costs and Related Matters: Since this committee had completed its assignment and its report accepted at the June 4th Council meeting, it was VOTED to discharge the committee with thanks.

CRMP CUPISS Technical Advisory Committee: It was VOTED to accept, with regret, and thanks for past service as a representative of CSMS on this Committee, the resignation of I. H. Friedberg, Newington. It was further VOTED that the President, in consultation with Marvin Garrell, the other CSMS representative on this Committee, submit names to CRMP for consideration as a replacement for Dr. Friedberg.

Date of Next Meeting

The date for the next meeting of the Council was set for Thursday, August 13, 1970.

IV. Old, New and Special Business

Report—Delegate to New Hampshire Medical Society

It was VOTED to accept, with commendation, a report filed by Stewart J. Petrie, Derby, Delegate to NHMS, on the proceedings of the Annual Meeting of the NHMS, Portsmouth, May 21-24, 1970. It was further VOTED that a copy of this report be sent, as information, to the Committee on Annual Meeting Arrangements.

Report—Delegate to the Massachusetts Medical Society

It was VOTED to accept, with commendation, a report filed by Frederick C. Weber, Jr., Greenwich, Delegate to MMS, on the proceedings of the Annual Meeting of the MMS, Boston May 26-28, 1970. It was further VOTED that a copy of this report be sent, as information, to the Committee on Annual Meeting Arrangements.

Requests for Expenditures

A series of recommendations of the Fiscal Advisory Committee were acted on as follows:

(a) It was VOTED to reimburse Stewart J. Petrie, Derby, in the amount of $77.16 for usual expenses incurred by his attendance, as a CSMS Delegate, at the 1970 Annual Meeting of the New Hampshire Medical Society.

(b) It was VOTED to reimburse Frederick C. Weber, Jr., Greenwich, in the amount of $13.30 for usual expenses incurred by his attendance, as a CSMS Delegate, at the 1970 Annual Meeting of the Massachusetts Medical Society.

(c) It was VOTED to approve the allocation of $250.00 to the budget of the Public Affairs Division to cover the costs of anticipated meetings.

(d) It was VOTED, in the light of increasing hospital costs, to approve the change of Blue Cross Coverage for CSMS employees from the Extended Plan to the Semi-Private Plan, at an additional annual premium of $336.00.

(e) It was VOTED to approve an additional allotment of $500.00 to cover anticipated costs of the "Congressional contact" visit to Washington, D.C., July 22, 1970. $1500.00 was allocated on June 4th, but in detailing the expense of this visit, it did not appear to be adequate.

(f) It was VOTED to approve the allocation of $250.00 to the budget of the Committee on Public Relations to cover the cost of a Press Conference to be held in the Fall of 1970.

Resolution Re Meetings of the CSMS House of Delegates

Considered by the House of Delegates on May 12, 1970, was a resolution, introduced by the Middlesex County Medical Association, which advocated more frequent meetings of the House of Delegates, or lengthier meetings or both, because of the ever-increasing volume of business. As a consequence, it was voted that the *semi-annual* meeting of the House of Delegates be increased from a half-day to a full-day, complete with reference committee hearings, and that the Council give further study to the format for *annual* meetings, in light of this year's experience and that of recent years; also, that the calling of meetings in addition to the two regular sessions be left to the discretion of the Council and the staff, depending on the amount and urgency of business to be brought before the House. It was VOTED that this subject be referred to the Committee on Annual Meeting Arrangements for study and report to the Council.

CSMS Relationships with CMS, Inc.

Since more than a year has passed since the House of Delegates directed the Council (in response to several county association resolutions) to investigate the feasibility and/or desirability of the Society resuming some sort of working relationship with CMS, Inc., and, further, that reports made to the Council by the Ad Hoc Committee on Liaison with CMS, Inc., indicated that no conclusions—even of a tentative nature—have been reached, it was VOTED that the Chairman of the Council be directed to communicate with CMS, Inc. requesting a statement as to whether a corporate relationship with the Society can be resumed and on what terms.

President's Advisory Committee

It was VOTED to approve the formation of a President's Advisory Committee to be appointed by the President. The membership of this Committee would be limited to six members in addition to the President, who would serve as Chairman. The purpose of the Committee would be to serve as a long range "planning and development" group which could develop goals and objectives, priorities, plans for County Association Officers Conferences, etc. The Committee would have no executive powers and would submit its recommendations, if any, to the Council for approval.

Liaison Committee with Welfare Department

The minutes of two meetings of the Liaison Committee with the Welfare Department were presented (1) Special meeting of CSMS committee held at 11:30 A.M., June 19th; (2) Meeting with Commissioners of Finance and Welfare at 1:30 P.M. on June 19th. It was VOTED to table action on this matter and the appointment of a Medical Advisory Committee until such time as the Society has some definitive information as to the type of program the Professional Policy Committee will develop based on the guiding principles set forth by the Liaison Committee.

Drug Abuse Educational Programs

The House of Delegates, at its meeting on May 12, 1970, adopted a resolution on Drug Abuse Educational Program which instructed the Council to appoint a committee of drug educators, more intensively trained in the principles of drug research and prevention of drug abuse, to carry out these educational programs. It was VOTED that Jacob P. deJong, Newtown, be appointed chairman of this Committee, and that he, in consultation with John Donnelly, Hartford, Chairman of the Committee on Mental Health, and Kurt Pelz, Wallingford, Chairman of an ad hoc committee (appointed by the Council on February 19, 1970, to study methods of preventing and controlling drug abuse among young people through making available to them voluntary counselling services), present to the

Council the names of members who might be interested in this activity. Such nominees, in addition to other members proposed by the Council, will be considered for appointment to this committee.

Medex Program

Dr. Pelz, Councilor from New Haven County, informed the Council that the Executive Committee of the New Haven County Medical Association, suggests that the CSMS make a study of the details of the "Medex" program now functioning at the Yale University School of Medicine. It was VOTED that this report be accepted as information and that it be referred to the Committee on Allied Medical Services for study and report.

Report—Committee on Public Relations

It was VOTED to accept a report and outline of operation, based on the minutes of a meeting held on June 18, 1970, which was presented by the Chairman, Dr. Root. It was VOTED to approve the following specific recommendations:

(1) That a press conference be held in the Fall of 1970. (The Fiscal Adivsory Committee has appropriated $250.00 for this conference).

(2) That Chairmen of CSMS Committees be informed that a master calendar of events is maintained by the Society in order to minimize conflicts among committee meetings, seminars, etc., and that committee chairmen should clear meeting dates with the CSMS office.

(3) That the Council approve the proposal that the committee chairmen of the Public Affairs Division be authorized to invite selected medical students from Yale University School of Medicine and the University of Connecticut School of Medicine to attend meetings of their committees. The Public Relations Committee suggested such medical students be obtained by contacting the Deans of the two medical schools in Connecticut.

Report—Public Affairs Division

It was VOTED to approve the holding of a Public Affairs Division Workshop on August 20, 1970. Dr. Burnham, Chairman of the Division outlined the program which would involve all of the Committees in this Division. The theme of the workshop would be political education. It was further VOTED to approve the estimated cost of $1000.00, to be appropriated from the funds allocated to the Council for political education, for this program.

Ad Hoc Committee on Health Care of the Poor

It was VOTED to adopt a recommendation submitted by the Ad Hoc Committee on Health Care of the Poor that CSMS urge its members to be active participants in the development and operation of health care plans for the poor in Connecticut. It was the understanding of the Council that the program for the implementation of this recommendation would be submitted to the Council at a later date.

Recommendations—Committee on Third Party Payments

It was VOTED to adopt the following recommendations submitted by the Committee on Third Party Payments:

(a) That individual insurance companies be asked to contact each physician for the purpose of obtaining his social security number and that the insurance companies put this number, as required, on each of the forms that the physician fills out.

(b) That the Council, through its properly constituted channels, inform the State Department of Welfare that the prior authorization forms that have to be filled out in order to obtain specialist care be discontinued by virtue of the fact that they are unnecessary and cause too much delay in the treatment of patients.

(c) That the New Haven Obstetrical Society and the insurance carriers be informed that it is the recommendation of the CSMS that obstetrical fees preferably should be based on usual and customary charges and that in any case, the fee paid for obstetrical services bear a relation to other surgical fees based on the Relative Value Scale of CSMS and, in addition, that new insurance contracts based on usual and customary charges should include coverage for obstetrics.

(d) That the Committee on Third Party Payments study the matter of cost analysis as it might relate to the practice of medicine.

COMPAC

It was VOTED to receive as information a report from Dr. Burnham, that an organizational meeting was held on July 14, 1970; that a new Board of Directors has been constituted; and that Dr. Burnham had been elected Chairman Pro-Tem.

N.B.: *The foregoing is a summary of the proceedings and actions of the Council on July 15, 1970. Detailed minutes of the meeting are on file at 160 St. Ronan Street, New Haven, for perusal by any interested member of the Society.*

What is worth doing...

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Average Adult Daily Dosage: One Gm. per day, in 4 divided doses of 250 mg. each. Should be given 1 hour before or 2 hours after meals, since absorption is impaired by the concomitant administration of high calcium content drugs, foods and some dairy products. Treatment of streptococcal infections should continue for 10 days, even though symptoms have subsided.

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281-0

New CSMS Staff Members

On June 1, 1970, two new assistant directors joined the Society's executive staff: Mr. Leonard R. Tomat and Mr. Raymond T. Sullivan, Jr. They are introduced to the membership herewith:

Leonard R. Tomat

Raymond T. Sullivan, Jr.

Mr. Tomat comes to the Society after ten years at Trinity College in Hartford, where he served as Associate Director for External Affairs. He formerly held the post of Assistant Dean of Students. He is a graduate (BA) of the University of Vermont and (MA) of New York University. Prior to his tenure at Trinity, Mr. Tomat taught school in Vermont and at the Riverdale Country School, New York City.

Married to the former Jean Hunter, an instructor at the Hartt College of Music, University of Hartford, Mr. Tomat, his wife and young son recently moved their residence from Windsor to 158 Alexander Drive, Meriden.

As Assistant Executive Director for Educational and Scientific Activities, his primary staff assignment is to those areas of CSMS activities.

Mr. Sullivan, until joining the Society's staff, held the post of Assistant Director of Development and Alumni Affairs at Boston College in Massachusetts. He has also had extensive business experience in the field of sales and sales promotion with several industrial firms. A graduate (BS) of Boston College in 1953, he also attended the Suffolk University Law School in Boston. He holds the rank of Lieutenant Commander (active) in the U.S. Coast Guard Reserve.

Married to the former Dorothy Kane of Jamaica Plain, Massachusetts, Mr. Sullivan, his wife and a majority of his seven children have moved from South Weymouth, Mass., to 27 Riverside Drive, Branford.

As Assistant Executive Director for Public Affairs, his primary staff assignment will be in the areas of legislative and socio-economic activities.

Council Approves Position Paper on Delivery of Medical Care for the State of Connecticut

On July 15, 1970, the Council approved the following position paper prepared by the Ad Hoc Committee on Delivery of Medical Care for the State of Connecticut. The document has been made available to all 1970 candidates for major political office in Connecticut. CSMS members may obtain reprints by contacting the Society headquarters in New Haven.

INTRODUCTION

In the public interest, the Connecticut State Medical Society feels it important to present its thoughts and recommendations on delivery of medical care to all candidates for political office in Connecticut. We hope this presentation will serve as an effective foundation for development of a sound health care program for all citizens of this state.

Many recommendations are rather broad—the Connecticut State Medical Society will be happy to provide more specific recommendations to any candidate who so desires.

Some subjects which are important are omitted from this report because final recommendations have not yet been formulated by the special committees considering them. Among such subjects are abortion reform, pollution, and drug abuse control.

As the conclusions on these subjects are obtained, they will be made available to anyone desiring them.

The Physician's Responsibility in Health Care:

Upon leaving office in January, 1969, former Secretary of Health, Education and Welfare Wilbur J. Cohen wrote to the nation's physicians: "The highest quality of medical service for all American people is (dependent on) freedom on the part of each individual physician to care for his patients in accordance with his best medical knowledge." While Mr. Cohen has never professed to be a close "friend" of the nation's practicing doctors, the Connecticut State Medical Society believes firmly that all levels of government should give careful and continuous heed to these parting words, i.e., that no matter to what extent governments may intervene financially in the delivery of health services, extreme caution should be observed to assure that the country's physicians are not regimented and do not have imposed on them regulations which interfere with the full exercise of their "best medical knowledge" in the care of patients.

Before the advent and expansion of tax-supported medical assistance programs, physicians and the hospitals with which they were associated, met the medical needs of the indigent and semi-indigent as a charitable community service. It was a "non-system," to be sure, but it got the job done reasonably well and at minimal cost to their fellow citizens. Except in the matter of personal patient-physician relationships, the patients received the same high quality of care as was available to all community residents. Most important, that non-system left to the judgment of doctors and hospital administrations the determination of what services and facilities were required to assure a uniformly high quality of care to all—wealthy and poor alike.

In the past two decades or so, however, the ever-increasing intervention of government has largely done away with this philanthropic method of caring for the less fortunate and has largely replaced it with a "system," or more accurately, with a whole series of "systems." There is one system for the elderly, another for the indigent, a third for the dependents of military personnel, a fourth for veterans, etc. While these various programs differ somewhat, one from another, they all have at least two characteristics in common: they were created by law, and their administrations have ultimately become bogged down in a morass of regulations which grows deeper with each passing year—regulations to control eligibility, regulations to control costs, regulations to control utilization, regulations to control quality, and, ultimately, regulations to control people.

Today, a variety of proposals are being advanced nationally for a government-operated "system" of health care for the entire population, and, should one of these be adopted by the Congress and implemented, the matter of administrative regulations will become of even greater concern to practicing physicians than at present. For this reason, the Connecticut State Medical Society offers a series of recommendations on the subject of government regulation of health care as follows:

(a) The determination of what services are "medically necessary" for optimum care of his patients should remain in the hands of the physician freely chosen by his patients. Government should not presume to assign patients to physicians or physicians to patients nor should it impose bureaucratic regulations on what services may be rendered by, or at the direction of the attending doctor. The Medical Society endorses peer review of both fees and utilization of services, but strongly advises against any requirement that medicine be practiced in accordance with a government manual of regulations.

(b) Assurance of high quality of medical services must be given precedence over considerations of cost at all times. There is a price for excellence in all goods and services—a price that must be paid for health if the full benefits of modern medical care are to be available to all citizens without exception. The Medical Society is not suggesting that proper accountability for the costs of quality health services be waived by either government or providers. It *is* suggesting that if cost control becomes of paramount concern to the funding agency, the quality of services is bound to deteriorate. As immediate consequences, medical progress will come to a halt, hospital facilities will become antiquated, underpaid personnel will become resentful or quit, and the ability of the health care "team" to deliver good care will thereby be seriously curtailed. As a long range consequence, it can be safely predicted that men and women of superior talents and intellects will ultimately seek careers in fields not so stringently controlled by government and will abandon the practice of medicine to persons of lesser qualifications.

(c) It is necessary for all concerned to accept the fact that industrial or business standards of efficiency can not be applied to the providing of medical and allied services. Since the need for these services is quite unpredictable, they must be maintained at full operating capacities twenty-four hours a day, seven days a week, whether they are called into use or not. Every citizen is entitled to expect, and *does* expect, that a full range of services will be available without delay when *he*, or a member of his family, is in need of them. The Medical Society endorses, and has given meaningful support to, measures which are designed to assure that medical and hospital services are used prudently to the end that their costs will remain at the lowest levels consistent with high quality. Though unmanaged medical costs are of vital interest to the Connecticut State Medical Society, it also expresses deep concern that non-medical planners might lose sight of the desired end, optimum care of all patients, and develop a new "system" of health care which will place undue and overriding emphasis on economy at the expense of practical and safe patient care.

(1) *Avoid regimentation that will make physicians unable to exercise their best medical knowledge in patient care.*

(2) *The determination of services that are medically necessary should be the responsibility of physicians only—not governmental bureaucracy.*

(3) *Peer review of fees and utilization review of services can only be provided effectively by physicians. It should be their responsibility and obligation to protect all patients from those few practitioners of medicine who make charges for medical care not in keeping with those made by other physicians for the same services, or who imprecisely call for tests, procedures or hospital bed usage which do not serve the best interests of these patients.*

(4) *High quality of medical services must not be sacrificed to cost control practices of funding agencies—although necessary service should be provided as economically as possible.*

Supply and Distribution of Physicians in Connecticut:

The supply of physicians in Connecticut today is quite good. In 1967, the year of the most complete recent study, Connecticut had one physician for every 860 Connecticut residents. This figure is significantly better than the national average of one physician for every 1,112 persons. These figures, however, do not reflect the problem of distribution in the state. For example, in Fairfield County there is one physician for 787 persons, while in Tolland County there is one physician for every 2,867 persons. Moreover, the number of general practitioners is declining more rapidly in Connecticut than in the country at large, and while the number of specialists is increasing it is not increasing sufficiently in internal medicine and pediatrics to make up for the deficit of general practitioners.

This indicates that unless something is done the people of Connecticut will find it increasingly difficult to get primary medical care. Also, since specialists' fees are higher than general practice fees, the cost per unit of physicians' services will go up.

As far as total numbers of physicians are concerned, three possibilities for augmenting the supply present themselves:

(a) Building new medical schools.

(b) Suddenly doubling or tripling student enrollment.

(c) Gradually increasing enrollment.

The first possibility is unworkable because there aren't enough funds available for this extensive construction, assuming necessary staffing is available.

For the same reasons, the second, suddenly doubling or tripling student enrollment, would seriously injure the quality of training for all and, therefore, would not be desirable.

The third, gradually increasing medical enrollment, is workable and should be encouraged as the necessary funds for construction and staff for teaching become available.

An additional suggestion includes training and utilization of paramedical personnel—similar to the army corpsman. These people could perform some of the technical tasks normally done by a physician and could thereby extend his effectiveness considerably.

To maintain the highest quality of care, while increasing the physician's efficiency, it is important to have such "physician assistants" closely supervised by the physician. Such assistants would, therefore, *extend* the physician's effectiveness but should *not replace* the physician or assume his ultimate responsibilities. Certification boards should be established and medico-legal questions answered to allow this development. Community colleges, universities, medical schools and hospitals could assume the responsibility for providing this paramedical personnel.

Problems of distribution might be handled by establishing groups in areas not presently having adequate numbers of physicians. These groups would have firm ties to nearby general hospitals. They would have working agreements with medical schools to have time off for refresher courses and/or vacations. They might choose to take a refresher course at the University of Connecticut School of Medicine or Yale Medical School and be replaced by residents provided by the medical schools. This would be mutually advantageous. Financial inducements if necessary might have to be provided by the state to insure an adequate income. Indentured governmental services such as army, navy, and similar organizations would be unacceptable and are not recommended.

Because the problems of the distribution of physicians to more rural areas is difficult, and has not been solved in other countries by merely increasing the number of physicians, easier access to medical care by various transportation mechanisms should also be considered.

Delivery of Medical Care:

In considering the medical needs of Connecticut, we must concern ourselves with the delivery system in medical care by which those needs can be met. We must endeavor, by all appropriate means, to make health services of high quality available to all individuals, in a dignified and acceptable manner, regardless of their social class, ethnic origin, ability to pay for services, or the source of the payments.

The Connecticut State Medical Society has the duty to guide and assist the medical profession in the attainment of this objective.

Medical care may be rendered either by individual physicians (solo practitioners) alone or in partnerships, in private offices or in an institutional setting. Or physicians may join together to form a group consisting of practitioners, all of whom are in the same field, or a multi-specialty group made up of physicians representing the various fields of medicine. Such a group may be private, medical school based, or hospital based. It may be a purely diagnostic group, or it may also engage in therapy. The group may be on a fee for service basis, or a prepaid basis.

The Connecticut State Medical Society opposes no system of delivery of medical care, and takes the position that local needs will determine which method is most suitable and which will render the best medical care.

It is generally assumed, and the idea is being promulgated by the federal government, that prepaid group practice must supersede all other delivery systems, but for large areas, this would not be feasible. That system is best which best serves the needs of any given locality. To give another system viability through propaganda or financial subsidy, is wrong.

(1) *Any plan or plans for delivery of medical care are acceptable which best suit the needs of any given locality.*

(2) *Forcing one delivery vehicle on a state or community wide basis through propaganda or financial subsidy is shortsighted and not in the best interest of the public to be served.*

Relationships of the State and the Medical Profession:

There are no areas of conflict between the State of Connecticut and practicing physicians insofar as stated objectives for medical assistance programs are concerned. That this is so was well demonstrated during the biennium 1967-69. As a consequence of the development of a close "working partnership" between representatives of the state administration and representatives of the medical profession (The Connecticut State Medical Society) one of the most effective and abuse-free Medicaid programs in the country was formulated and put into operation. The one "pilot year" (3/1/68-3/1/69) of payment for physicians' services on the basis of "usual and customary charges" proved beyond any question that such a partnership could achieve desired ends; i.e., cost per service was reasonable; the program operated within the budgeted funds allocated; it was free of abuse, due to the review activities of a Medical Advisory Committee (furnished by the Medical Society); the number of beneficiaries receiving quality care on a private basis doubled and the number of services, provided by both generalists and specialists, increased manyfold; the number of practitioners participating in Medicaid increased from 300 or so (as of July 1967) to more than 3,000 (as of March 1969). In summary, this highly successful and highly praised program enabled some 170,000 needy and near-needy people in Connecticut to obtain, for the first time, medical care of high quality on the same footing as their more fortunate fellow citizens, from private physicians of their own choosing.

The objectives of the Connecticut State Medical Society regarding Medicaid remain unchanged. Unfortunately, the 1969 General Assembly felt it necessary to drop out of partnership with the medical profession by *not* acting to continue the program beyond March 1, 1969. It is the hope of the Society that the next Administration and the next legislature will elect to rejoin the partnership and work with the Society to restore the type of program which held such great promise when it was terminated. The Society re-pledges its cooperation toward that end.

In addition to working cooperatively with the Departments of Welfare and of Finance and Control, as just recounted, the State Medical Society has always enjoyed an enviable two-way relationship with the Department of Health and the Department of Mental Health which has led to the development of programs of benefit to the public and agreeable and helpful to practitioners.

Such areas of conflict as exist between the State of Connecticut and physicians are created, in general, when our legislators lend too attentive an ear to non-medical health care planners and too inattentive an ear to the advice of medical practitioners. It is one thing to draw up a program based on theory and quite another to make it work in practice. Today, some people are even saying that "medical care is too important to leave in the hands of doctors." The Connecticut medical profession does not claim to have ready and complete answers to all questions pertaining to health and health care. It does claim, however, to have considerable expertise in the delivery of patient care and feels strongly that its views should be taken into full account *before* legislative and regulatory decisions are made.

(1) *The desires of the state, the consumer and the physicians should be weighed in consideration of any plan for Medicaid in Connecticut.*

(2) *The experimental plan used during the pilot year* 3/1/68-3/1/69 *was successful in all respects and it, or some modification of it, should be seriously reconsidered during the next session of the General Assembly.*

Relationships of Physicians and Insured Patients:

What is the relationship between physicians and their patients who are enrolled in third party payment plans? The answer is that, in general, a majority of physicians participate voluntarily in all or most of these plans. Such voluntary participation by the majority indicates clearly that the concept of third party payment is subscribed to by most physicians. Also, in general, it may be said that the patient-physician relationship is not intruded upon by responsible third party payors. Those that do intrude are not satisfactory to either the physician *or* the patient.

Since their inception, the professional organizations of physicians have provided a mechanism for recourse in the event that a patient was not satisfied with a service rendered or a charge made for same by a physician member. In recent years, the expansion of the third party payment method of paying all or part of a physician's fee has prompted these organizations to develop mechanisms for "peer review" which work cooperatively with third parties, both in the area of charges made and of utilization of covered services. Operating effectively and without fanfare in the private sector, such review committees have contributed greatly to the prudent disbursement of third party funds. In the public sector, the efforts of the Medical Advisory Committee that provided peer review to Connecticut's Medicaid program during most of the 1967-69 biennium (especially during the 12-months trial of the "usual and customary charge" method of payment) was largely responsible for the fact that the program was practically abuse-free, was economical as to cost-per-service, operated well within its allocated budget, and, at the same time, made it possible for thousands upon thousands of the needy and near-needy to obtain, as private patients, medical care of high quality, many for the first time in their lives. To be repetitious only for the sake of emphasis, it remains difficult for the profession to understand the decision of the 1969 General Assembly to discontinue a Medicaid program of such proven merit.

In the opinion of the Connecticut State Medical Society, the growth of private, voluntary health insurance and prepayment plans should be encouraged by government at all levels, and, in the event that Federal tax-funded health service coverage is legislated for all citizens, those private plans, their vast experience and their proven ability to work cooperatively with the medical profession should be utilized to the fullest in implementing such a Federal program.

Also, in the Medical Society's opinion, encouragement should be given to third party payors, both private and public, to improve their plans along the following lines:

(1) *Provide coverage for all services which can be rendered by the physician in his office or other outpatient setting, thereby eliminating the need for expensive admission to hospitals in order to qualify for benefits payments.*

(2) *Move in the direction of paying "reasonable" charges for physicians' services, rather than paying indemnities (which are often inadequate and disappointing to patients) or using uniform (statewide) "fixed" payments which may be grossly substandard in many parts of the state. Peer review can be most effective when "reasonable" charges are honored for payment. Conversely, peer review by physicians of payments is of little value when such payments are indemities or based on a "fixed" and oftentimes obsolete fee schedule.*

(3) *Move away from operating policies that insist that physicians practice "by the book;" that "prior authorization" must be obtained from the payor before a service can be rendered; that drugs can be prescribed only if they are on the payor's list; that either limit the number of visits or treatments allowed or require that the patient be seen at stipulated intervals; etc. These are limiting and self-defeating controls when applied to the imprecisions of patient care. They work effectively in other areas of budgetary limitations where products or services can be standardized, but when applied to the multitude of variances inherent in medical care become inhibitory and, in some cases, deleterious to the welfare of human beings.*

RECOMMENDATIONS FOR "GOVERNOR'S COUNCIL"

Not infrequently, governors in the past, when faced with major decisions on health care issues, have been subject to many conflicting opinions, some of which have been biased and based on inadequate knowledge. Because the medical profession feels that the governor should be fully and accurately informed on issues in health care which will require his decision and which will affect the care of state residents, it is recommended that:

The governor should have available to him an advisory council, consisting of people knowledgeable in the health care field, including physicians in the private practice of medicine. The Connecticut State Medical Society would be pleased to nominate qualified physician members to such a council, from which he may make a selection.

Presented by the Ad Hoc Committee on Delivery of Medical Care for the State of Connecticut.

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Special Article

Medicine In Israel

Ned Thomas

BEER SHEBA, Israel—Although Israel has the highest ratio of doctors in the world, one of its leading physicians asserts that the fledgling country could still use more physicians.

Dr. Joseph Stern, director of the Negev Central Hospital and head of one of the hospital's medical departments, contends there is a shortage of general practitioners in the country.

Dr. Stern, who was a visitor at the gastrointestinal department at Yale University Medical School a few years ago, as a guest of Dr. Howard Spiro, feels that the country, whose population equals that of Connecticut, could use another 500 G.P.'s.

He says that 90 per cent of the doctors in Israel try to become specialists in one field or another. Very few physicians, he adds, choose to remain general practitioners.

Those who wish to become physicians in Israel must complete six years of medical school and one year of internship, after which they can practice medicine. However, the vast majority of them spend another five to six years full time specializing in their field of choice in hospitals.

Currently, the ratio of doctors in Israel is one to each 500 persons. Most of them are concentrated in the big cities, such as Tel Aviv, Jerusalem and Haifa, resulting in doctor shortages in the smaller towns and villages of the holy land.

Thus, the ratio in the new and bustling city of Beer Sheba is one doctor to every 2,000 persons, which is considerably below the national average for the whole of Israel. (In the U.S., the ratio is one physician for every 600 and some residents, but the ratio drops down in the small communities, just as it does everywhere else in the world.)

Another aspect of the picture here is that a high number of physicians are above the age of retirement. The retirement age is 65 for men and 60 for women: who constitute 10 per cent of the doctor force.

It is expected, Dr. Stern says, that Israel's ratio of doctors will fall sharply as most of those in the overage bracket retire from the profession in the next 10 years.

Israel acquired the high ratio with the inflow of doctors from Western Europe. Some came here before World War II, but many more emigrated here after the war.

A large percentage of the Israeli physicians are affiliated with prepaid medical plans. According to Dr. Stern, more than 70 per cent of the Israel people are covered by a comprehensive prepaid medical plan, sponsored by the Sick Fund of the Histadrut of the Jewish Labor Federation. It is called Kupat Holim.

The remaining 30 per cent are serviced by various private prepaid medical insurance plans and by private physicians.

Every member of the Sick Fund, Dr. Stern says, has free access to clinics, specialized clinics and hospitalization, as recommended by the treating physicians.

Those requiring hospitalization can be admitted to a Kupat Holim Hospital, run by the Histadrut, or to a government hospital.

While most physicians are active on a full time basis in the Sick Fund plan, many of them also see private patients. Hospital physicians are on a full time basis, however, except a number of heads of departments who have permission to engage in private practice.

In the large cities, particularly in Tel Aviv and Jerusalem, there are a number of private physicians, but in the villages and smaller towns there are very few.

The Negev Central Hospital, built by the Sick Fund, serves all of the population in the Negev area, which has a population of about 200,000, including 20,000 Bedouins.

About 90 per cent of the population in the Negev belongs to the Sick Fund. A member of the General Jewish Labor Federation is automatically a member of the Sick Fund.

MR. NED THOMAS is a medical science writer for the New Haven Register.

The Negev Central Hospital serves all of the population in the area, irrespective of membership in the Sick Fund. The Bedouins are serviced at the hospital through special arrangement with the Israeli Government Department of Health.

Lately, however, quite a few Beduoins joined the Federation and are entitled to free treatment at the hospital.

"No one," Dr. Stern declares, "is refused medical treatment at the hospital, if he needs it, regardless whether he can pay for it or not, and whether or not he is a member of the Sick Fund."

If a man is poor and cannot pay for hospitalization, the municipality pays for it.

Dr. Stern explains that clinics serve as the patient's physician, but the patient usually sees the same physician at the clinic. Each settlement usually has its own clinic.

The Negev Central Hospital has 100 full time doctors and 530 beds, having doubled the number of beds in the last 10 years. The hospital plans to enlarge its number of beds to 800 in the next five years.

In Beer Sheba patients have a waiting period of several weeks when elective surgery is recommended but when it involves eye surgery, the patient may have to wait several months.

Dr. Stern explains that many chronic eye illnesses have been brought into Israel from North Africa, such as the sequella of trachoma and senile cataracks.

Patients admitted to the hospital are treated by the permanent staff. While the referring physician may visit the patient, he does not treat him in the hospital. After discharge, the patient is referred again to his clinic physician.

Dr. Stern observes that the clinic physicians are "not too happy" about this arrangement.

To remain on "the inside," as it were, the clinic physicians stay a half day a week in the hospital. This gives them the privilege of visiting their patients in the hospital and discussing their condition, treatment and progress with the hospital doctors. They can even suggest specific treatment for their patients, when they think it is warranted.

The clinic physicians also attend lectures at the hospital and make rounds. It is during the latter period that the clinic doctors have the opportunity to discuss their patients with the hospital doctors.

"This procedure," says Dr. Stern, "gives the patients the feeling that their clinic doctor is not an outsider."

Clinic doctors are also repaid through the opportunity to attend special courses given periodically by and at the hospital to keep doctors abreast of the latest developments in different branches of medicine.

Dr. Stern notes that while the Kupat Holim controls only a third of the hospitals, it treats 80 per cent of the patients needing hospital care in the country.

Most general hospitals in Israel are also teaching hospitals, affiliated with one of the two medical schools in the country. The two medical schools are Hebrew University Medical School in Jerusalem and the Tel Aviv University Medical School.

By the end of 1971, Stern says, the Negev Central Hospital will become a teaching hospital of the medical school to be established here. In addition, a new university medical school is currently being organized at Haifa and has already accepted students for the fourth year of medical school study.

What about patients who require medical care at night? For those who need the attention of a physician at night, Dr. Stern says, there are physicians on duty at specified clinics from 8 to 12 p.m. He adds that most clinics require patients to come to it, but he adds that there are also house calls for those who cannot come to the clinic.

There are very few house calls made after midnight. In the big cities, there is a first aid Mogen David Red Cross station where a physician is always on duty to cope with emergencies. The more serious cases are referred to the hospital.

Because of the undeclared war between Israel on one side and Egypt and other Arab states on the other, the hospital in Beer Sheba has been making use of helicopters to fly in wounded soldiers, especially since the Six Day War of 1967. The hospital has an area set aside for the landing of helicopters on its own grounds.

Comparing the quality of medicine practiced in Israel with that in the United States, Dr. Stern says that whereas there are both "high and low qualities of medicine practiced in the U.S., each person in Israel gets an average good quality of medical care irrespective of his or her income."

Electrocardiogram of the Month

Yale-New Haven Hospital
New Haven, Connecticut

Prepored by
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Misapplication of the limb lead electrodes will result in an abnormal appearance of the electrocardiographic complexes in some or all of the limb leads and may lead to an erroneous diagnosis of pathology when none exists, or to erroneous localization of pathology when it does exist. The correct localization of the site of infarction may be of clinical significance since complications such as cardiac arrest due to tri-fascicular block (bilateral bundle branch block) occurs more often when the infarction is anterior septal in location, whereas papillary muscle dysfunction and rhythm disturbance such as marked sinus bradycardia, sinus arrest, A-V conduction disturbances, and AV dissociation may be anticipated when the inferior or posterior wall is the site of the infarction. Such errors in diagnosis can be avoided since there are a number of clues which should make the reader suspect misapplication of the limb lead electrodes.

The most common technician's error made is the reversal of the right arm and left arm electrodes. Since lead I measures the difference in potential that exists between the left arm and the right arm, the reversal of the electrode application results in lead I exihibiting a mirror image of itself. (Fig. 1A). The combined finding of an inverted P-wave, downward directed main QRS deflections, and inverted T-waves in lead I should make one suspect electrode misapplication rather than an anterior wall infarction. Inspection of the P-QRS-T patterns in leads VR and VL will reveal that these leads are interchanged. In the rare instance of dextrocardia these leads will also appear to be interchanged. Inspection of the chest leads will help differentiate dextrocardia from technician's error since in the case of the dextrocardia the chest leads will not exhibit the normal progression of R-wave amplitude from right to left. Repeat tracing with proper application of limb leads reveals normal tracing (Fig. I B).

A less common technician's error is interchanging the left arm and left leg electrodes. Lead 3 measures the difference in potential between the left leg and the left arm and as a consequence of the error will appear as a mirror image of itself. Since lead 3 may normally exhibit an upright T-wave, an rS complex and an upright T-wave, the mirror image of this results in a qR complex with an inverted T-wave which may lead to the erroneous diagnosis of a past inferior wall infarction. Recently such a technician's error resulted in the tracing shown in Fig. 2A, obtained in a patient admitted to the hospital suffering from severe chest pain. Inspection of the chest leads revealed the classic patterns found in infarction of the anterior wall. However, inspection of the limb leads as recorded revealed patterns characteristic of infarction of the inferior wall. A technician's error was suspected because the P-waves were noted to be normally inverted in lead AVR (as should occur if the patient had sinus rhythm), but the P-waves were noted to be inverted in leads 3 and AVF (which should not be the case if sinus rhythm was present.) Inspection of the P-QRS-T patterns in leads VF and VL as recorded revealed an interchange of these two leads. Repeat tracing the following day with limb lead electrodes properly applied exhibits normal sinus rhythm with upright P-waves in leads 3 and AVF and classic patterns of anterior wall infarction in all leads and no evidence of a co-existing inferior wall infarction (Fig. 2B).

Rarest of all technician's errors is misapplication of all three of the limb lead electrodes. This results in an unusual appearance of leads 1, 2, 3, and AVR (Fig. 3A). In this case the right arm electrode was mistakenly placed on the left leg, the left arm electrode was placed on the right arm, and left leg electrode was placed on the left arm. The tracing as recorded revealed patterns in the limb leads which had the appearance of a recent anterior wall infarction. However, the chest leads were consistent with an injury current arising in the inferior wall. The error in lead placement was suspected because of this discrepancy and because of the presence of inverted P-waves in leads 2, 3 and AVF while the P-waves in the chest leads were normal upright. The chest leads are unaffected by the total misapplication of the limb lead electrodes since during the recording of these leads the 3 limb lead electrodes are shunted together in the electrocardiographic apparatus to form a common terminal. When the tracing was repeated with proper application of the limb lead electrodes, the patterns of a recent inferior wall infarction were present in the limb leads and the chest leads (Fig. 3B), and the P-waves were of a normal polarity in leads 2, 3 and AVF. There was no evidence of an associated anterior wall infarction.

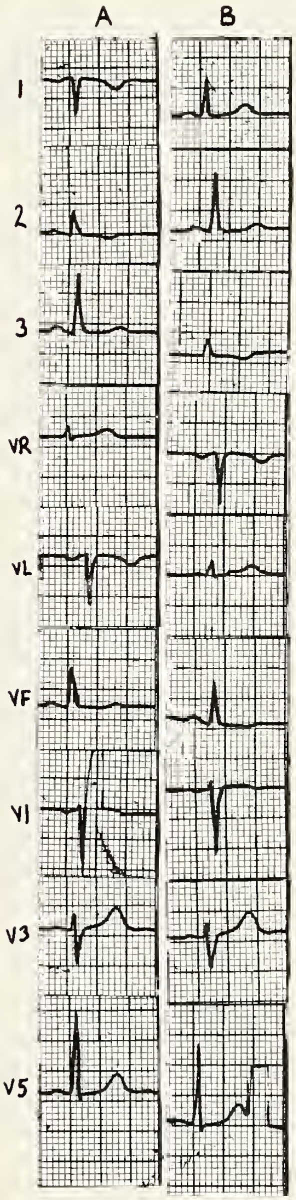

FIG. 1

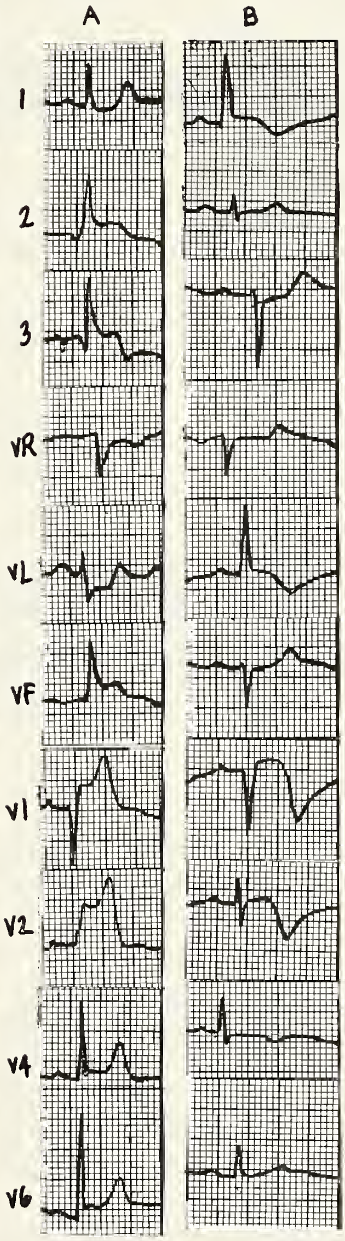

FIG. 2

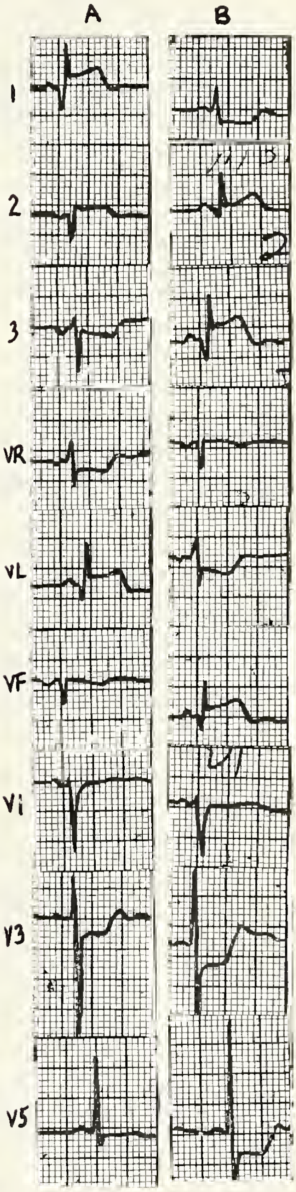

FIG. 3

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Medical Grand Rounds At Yale-New Haven Hospital

Septic Abortion

Frederick Lee Sachs, M.D. and Lewis Landsberg, M.D., Editors
Pamela Brooten, Assistant Editor

The patient is a 17 year old gravida 1, para 0, single white girl who was transferred to the Obstetrical Service of the Yale-New Haven Hospital from the Meriden Hospital one week ago because of high fever and red urine. Her last menstrual period was 3 months ago. Two days before admission she consulted an abortionist who injected a watery material transvaginally into her uterus in an attempt to induce an abortion. That evening she began to have severe abdominal cramps and the day before admission she passed a fetus and bled heavily from the vagina. The night of admission she passed red urine and was taken to the Meriden Hospital where she was afebrile but still bleeding. A dilation and curettage was performed and a small amount of tissue was obtained. In the recovery room her temperature rose to 104 degrees. Urinalysis revealed only 0-3 red blood cells per high power despite the fact that her urine was quite red. She was begun on antibiotics and mannitol and transferred to the Yale-New Haven Hospital. On admission her blood pressure was normal but the temperature was 105. Her pulse was 156 and regular. She was pale and acutely ill. Pertinent physical findings included S3 and S4 gallops and clear lung fields. Her abdomen initially was tender in the lower quadrants but several hours after arrival she developed diffuse abdominal pain and tenderness. Culdocentesis revealed bloody fluid. The uterus and adnexae were extremely tender on pelvic examination.

On admission the hematocrit was 34% which was unchanged from that at Meriden. Urinalysis showed 0-2 red blood cells with free hemoglobin in the urine. Her white blood count was 46,800 with a shift to the left. Platelets were adequate on smear but there was prolongation of the prothrombin time to 41.5 seconds. The fibrinogen was 410 mg%. The BUN was 56 mg% with a creatinine of 2.5 mg%. Serum electrolytes revealed the bicarbonate to be 16.2 meq/l, chloride 92 meq/l, sodium 117 meq/l, and potassium 4.1 mq/l. Liver function studies showed a total bilirubin of 1.05 mg%, direct 0.53 mg%. The SGOT was 245 units and the alkaline phosphatase 73 International Units. Clostridium Perfringens and Staphylococcus Aureus were grown from the uterus and cervix. Blood cultures were negative.

Because of her high fever and acute abdomen she was taken to the operating room where a necrotic left uterine cornual area was discovered. The ovaries and left fallopian tube were black and necrotic. A total abdominal hysterectomy and salpingoophorectomy was performed.

Post-operatively the patient developed a number of significant problems. Her PO2 gradually fell after surgery and a friction rub was heard on the left chest with signs of consolidation. We believed that she had had a pulmonary embolus with infarction and heparin was administered on this premise. Her temperature rose the day after operation and remained elevated. There were several abnormalities in her coagulation studies. The Partial Thromboplastin Time was prolonged to 41.5 seconds on the day of admission and the next day it rose to 96 seconds, returning to 31.5 seconds on day 4. On day 2, her prothrombin time fell to 15.2 seconds, and was 13.6 seconds by day 3. Her fibrinogen level dropped and her platelet count was 84,000. She was given 5 units of whole blood on the third postoperative day because of intra-abdominal bleeding as evidenced by an enlarging abdomen, drop in central venous pressure and rapid pulse. The heparin was reversed with protamine. After the transfusions the bleeding seemed to abate and there was a return towards normal in her coagulation studies. The thought was that the initial bleeding was due to a consumptive coagulopathy but that the heparin had led to more profuse abdominal bleeding.

DR. FREDERICK LEE SACHS, Assistant Professor of Medicine, Yale University School of Medicine, New Haven, Conn.

DR. LEWIS LANDSBERG, Assistant Professor of Medicine, Yale University School of Medicine, New Haven, Conn.

Renal problems were significant as her BUN was 57 mg% on admission. This was treated with a mannitol and Lasix diuresis. On this regimen her BUN slowly dropped to 15 mg% one week after admission. Her creatinine has remained above 2 mg%, however. The electrolyte abnormalities seen on admission were corrected with intravenous NaCl and her electrolytes are now normal.

DR. YALE NEMERSON: Was the fibrinogen level of 100 mg% measured while the patient was on heparin? This is an important question because if the laboratory was not told that the patient was on heparin, the measurement obtained was almost certainly artifactual since the determination is made as thrombin clotable protein by the lab.

DR. COUSTAN: The value of 100 mg% was obtained with the patient on heparin. I do not believe that the laboratory was informed of that fact before this determination but they did know of this fact for subsequent determinations and added protamine.

DR. STUART FINCH: Did the bilirubin ever rise?

DR. COUSTAN: The high for the total bilirubin was 1.08 mg%.

DR. LEWIS LANDSBERG: Dr. Ronald Hoy will review the x-rays.

DR. RONALD HOY: A portable chest film taken soon after admission was normal. Shortly afterwards, on the same day, a repeat film revealed abnormality in the lower lung fields with air bronchograms seen bilaterally. There has not been a great deal of change in the chest films. We cannot diagnose the cause of the air bronchogram. It could be due to infection, but it certainly is not diagnostic.

DR. LANDSBERG: Dr. Irving Friedman operated on this girl and will describe some of the operative findings and operative considerations.

DR. IRVING FRIEDMAN: It is often extraordinarily difficult to get a good history in a case of criminal abortion. In this instance we knew that some type of liquid had been injected into the uterus. There was some talk as to whether Lysol had been used but we were not sure. This question of how the abortion was actually carried out is of more academic interest because although criminal abortions all have in common the factor of infection, an abortion produced by Lysol or soap is a very different entity from that produced by the use of a dirty catheter. The difference is that Lysol produces an area of tissue necrosis and, in addition, is absorbed into the bloodstream. The necrotic tissue serves as a nidus for infection. Infection in such damaged tissue is immune to the effects of systemic antibiotics because the antibiotic can't get to it. The type of organism which grows in this medium may be endotoxin producing gram negative bacteria or it may be an anerobe such as tetanus. The part which is absorbed into the bloodstream is nephrotoxic, hepatotoxic and produces hemolysis.

The uterus is an extraordinarily vascular organ in pregnancy. In this instance we thought that we were probably dealing with a case in which Lysol was injected producing its local effect on myometrium and its systemic effects by absorption into the bloodstream. The patient was operated on some 60 hours after the injection had been performed. Her temperature had risen to 105° in spite of therapy with penicillin and Kanamycin. The uterus which was initially tender was now enlarging and there were signs of general peritoneal irritation. In addition, the culdocentesis indicated that there was a gangrenous organ in the abdominal cavity. We therefore had no choice but to remove the uterus and ovaries when, at surgery, they were all found to be gangrenous.

DR. LANDSBERG: Are there any questions for Dr. Friedman?

DR. PHILIP K. BONDY: I wonder if Dr. Friedman would expand his comment about what you would have expected if a soap solution had been used. The main toxic element of Lysol, I suppose, is phenol; what about these other compounds?

DR. FRIEDMAN: Detergent and soaps resemble Lysol in their effects.

DR. PATRICK McKEGNEY: Was there any possibility of finding out who did the abortion?

DR. FRIEDMAN: Yes. The patient's parents were most cooperative. The woman who was named as the abortionist was known to the police. She was involved with a fatality in a similar case six months earlier.

DR. STUART FINCH: What is the usual interval between the criminal intervention and the onset of hemolysis or infection?

DR. FRIEDMAN: Hemolysis occurs quickly as the injected agent enters the bloodstream. The myoglobin does not appear until later.

DR. SAMUEL SPINNER: How much of this reaction would you relate to the nature of the infecting organism?

DR. IRVING FRIEDMAN: This is a difficult question to answer because given a necrotic organ with a Welch Bacillus infection, it is difficult to describe certain effects to the necrosis and others to the infecting organism. I do believe, however, that the infection does play a dominant role. It is difficult to cope with this infection as long as one is dealing with a large area of necrotic tissue.

DR. STUART FINCH: I should like to point out that with cases of this type there may be two sources of hemolysis. Initially, hemolysis may be caused by the Lysol as it enters the bloodstream. A second phase of hemolysis may occur some 24 to 48 hours later when the alpha toxin of the Welch Bacillus is released as the infection progresses.

DR. COUSTAN: Support for Dr. Finch's statement may come from the patient who relates that she had red urine immediately following the abortion but that this cleared only to return again some 36 hours later.

DR. LANDSBERG: Dr. Lawrence Freedman will discuss some of the implications of this case.

DR. LAWRENCE FREEDMAN: I would like to discuss the infectious complications by first reviewing some of the epidemiology involved. In a recent issue, the British Medical Journal (1) published data concerning the incidence of therapeutic abortion and criminal abortion in the years 1961-1967. The figures indicate that there are about 25 deaths each year due to criminal abortion. There was a significant increase in the number of therapeutic abortions prior to 1967 when the British passed their latest abortion law. In 1961, 2,280 abortions were performed, contrasted with 7,610 in 1967. I believe that this increasing incidence illustrates the social pressures that were at play before the passage of this new law. The key passages of the new law state that termination of the pregnancy would be lawful if "continuance of the pregnancy would involve threats to the life or injury to the health, whether physical or mental, of the pregnant woman, before or after birth of the child". It was reasoned that since the threat of carrying a pregnancy to term was greater than the risk of a therapeutic abortion, any pregnant woman who desired an abortion had the right to receive one. The data for the first year after the passage of the law indicate that 41,495 therapeutic abortions were performed in Britain without mortality.

Studies done in the state of Michigan between 1950 and 1965 indicate that the second most common cause of maternal mortality is puerperal infection and that septic abortion is the leading cause of puerperal infection. In Detroit, 662 cases of septic abortion occurred within a two year period. Twelve patients were admitted in shock and there were two deaths, for a mortality rate of 1 in 331 cases. The incidence of death following septic abortion is quite low.

We have no reliable data on the incidence of criminal abortion but some estimates run as high as one and one-half million per year. Some postulate that in the United States, one in five pregnancies is aborted. In Japan, where abortion is legal, there are more therapeutic abortions than live births.

One difficulty in studying septic abortion is that the definitions of septic abortion are poorly established. The series of Moritz and Thompson,[2] published in 1966, uses the criteria of a "bleeding pregnant patient who presents with one or more of the following: 1) history of criminal intervention; 2) temperature of 100 degrees orally; 3) salmon-pink, foul-smelling uterine discharge; 4) pelvic or generalized peritonitis; 5) white count of over 15,000." Weingold's[3] criteria includes "abortion, temperature elevation, and positive blood cultures". They reported 43 patients. The organisms involved included gram negative and gram positive organisms. Two anerobes are mentioned in these 43 patients, both of which were Clostridium Welchi. Their deaths occurred in patients with Welch Bacillus or gram negative rods. In January of 1969 Rotheram and Shick[4] published a classic paper which brought to bear the techniques of anerobic bacteriology on the problem of septic abortion in some systematic way. Their selection included all patients discharged with a diagnosis of septic abortion over a two year period. They then subjected these 95 cases to the criteria of: 1) fever and chills by history; 2) a recorded temperature equal to or greater than 100.5°C; and 3) microscopic confirmation of gestation less than six months. Eighty-seven patients met these criteria. Fifty-six of these 87 had admission blood cultures of which 34 or 60% had positive cultures. Using the techniques of anerobic bacteriology they were able to detect that 64% of these patients had only anerobic or microaerophilic organisms in the blood. Three of them had mixed anerobic infections and 8 patients were found to have aerobes alone in the blood cultures. If their data can be reproduced at other centers then we must reorganize our thinking about septic abortions along the lines of improved anerobic techniques. The bacteria including streptococcus, the three species of bacteroides, and micrococci. A total of 34 cultures contained those organisms. The microaerophilic organisms included streptococci, hemophilus vaginalis, and actinomyces. The aerobic organisms include *E.*

Coli, Group B and Group D streptococci, pseudomonas, and a Diptheroid.

The problem of assigning causality to a particular organism with regard to the complications of the disease is even more complex because anerobic bacteria are normal inhabitants of the vagina. Therefore, unless carried out with particular care to protect the collecting object from the environment of the vagina, vaginal or cervical cultures would be apt to show organisms which might have no role whatsoever in the pathogenesis of the disease. In the classic case of Welch Bacillus septic abortion reported by Drs. Isham and Finch[3] one of the interesting aspects of the case was the fact that after 8 days of penicillin in a girl with renal insufficiency whose blood levels of penicillin must have been quite high, the Welch Bacillus was cultured from the uterus after death. This emphasizes Dr. Friedman's point that if you have a necrotic organ with a sensitive organism, antibiotics alone will not eradicate the organism.

Pelvic abscesses are a common complication of septic abortion and this patient may well have developed one. Metastatic abscesses are a major problem especially in cases of Bacteroides where lung complications are frequent. Tetanus is also a complication not to be overlooked.

DR. LANDSBERG: Dr. Franklin Epstein will comment upon some of the renal complications that occur in this disease.

DR. FRANKLIN EPSTEIN: One of the major causes of death in patients with septic abortion is renal insufficiency. In any series of patients with acute tubular necrosis or cortical necrosis one sees a large percentage of patients who have had septic abortion. The kidney of a pregnant woman seems to be susceptible to the kind of insult that gives rise to tubular necrosis and cortical necrosis. It is not clear why this is so. It may be related to two known physiological concomitants of pregnancy. In the first place the renal blood flow, for reasons which are not well understood, increases greatly from the very first months of pregnancy to 50% above normal. This may exert an effect by increasing the delivery to the kidney of the toxic substances circulating in the blood after the septic abortion. In addition, the kidney in pregnancy is susceptible to the effects of a generalized Schwartzman reaction. The hallmark of the generalized Schwartzman reaction is cortical necrosis. This can be induced, for example, in a nonpregnant rabbit by initial injection or sensitizing injection of gram negative endotoxin followed by a subsequent injection which produces the Schwartzman reaction and renal cortical necrosis. I think it very significant that if you have a pregnant rabbit, it just takes a single injection of gram negative endotoxin to cause cortical necrosis. This may be why cortical necrosis and acute tubular necrosis are such common accompaniments of septic abortions.

The important question is what to do to prevent ischemic tubular necrosis in such a patient. It would seem logical to do two things. First, we should attempt to diminish the concentration of toxin in the urine, and, second, we should increase the renal blood flow by whatever means we can, since renal ischemia is an important factor in producing tubular necrosis and the renal shutdown. Hemolysis itself is an important cause of necrosis. The globin part of the hemoglobin molecule as well as other factors present in hemolyzed red blood cells themselves are very powerful renal vasoconstrictors. The thing to do then is to reestablish the circulation, prevent the shock, and induce a copious dilute urine flow so that whatever toxins are present will be diluted in the renal tubule. The best way to accomplish these ends is to induce a generous diuresis with mannitol. Furosemide may be added although we are not sure that it is effective; this diuretic is of interest in that it increases renal blood flow whereas chlorthiazide decreases it. So far no one has been able to show that injections of mannitol are more effective in preventing tubular necrosis than injections of large amounts of saline. Nevertheless, what we do in fact is to support the circulation with transfusions, and give 50 grams of mannitol to induce a mannitol diuresis, hoping that this will mitigate the toxic effects of septic abortion.

DR. LANDSBERG: Dr. Morris, do you have any comments?

DR. JOHN McCLAIN MORRIS: Between 1965 and 1969 we had 19 cases of septic shock on our service, of whom 9 died. At Yale-New Haven we consider hysterectomy a satisfactory alternative to the development of septic abortion with shock. The reason we say this is that we carefully studied the specimens that we have removed, and with one exception, the tissue removed was so diseased that it was apparent that had it remained, it was not compatible with the survival of the patient. I have always scoffed at the concept of emboli coming from the ovarian vessels. However, the ovarian veins in some of these organs were so large that they measured over 2 cm. in diameter. The uteri were black, necrotic, foul-smelling organs. The criteria which we set up in the decision to perform hysterectomies were: 1) The use of detergents or pine tar derivatives; 2) Failure to respond to more conventional methods. In other words, if we treated the patient and there was a failure to respond satisfactorily, then hysterectomy was performed. 3) A large tender uterus. I am most pleased that this patient underwent hysterectomy. The fact that she was a 17-year-old girl made the decision difficult, but I do not believe that there was any alternative choice open.

DR. LANDSBERG: Dr. Nemerson will comment on some aspects of the coagulation abnormalities.

DR. YALE NEMERSON: The original data showed a long prothrombin time and normal Partial Thromboplastin Time. This might bear on an observation made a few years ago by Dr. Rappaport of UCLA. He noted that in patients with meningococcemia there is often an isolated depression of factor VII which is involved only in the prothrombin time. The reason for this isolated depression is somewhat obscure. It may be related to the fact that the half life of factor VII is very short, in the neighborhood of two hours. Consequently, any suppression of protein synthesis due to a hepatotoxin would be reflected first in a prolongation of the prothrombin time. Other tests of clotting function would remain normal for perhaps two or three days. I suspect that this may have happened in this patient. The thrombocytopenia is not necessarily a reflection of intravascular coagulation. It may also be explained by the fact that bacteria, viruses, and certain toxins may attach to platelets and cause their rapid removal from the circulation. When faced with a thrombocytopenic patient, one should always remember to reduce the dose of heparin because platelets inactivate large quantities of heparin and, therefore, with reduced levels of platelets it is possible to administer too much heparin if standard doses are used.

DR. LANDSBERG: Are there any further comments?

DR. FREDERICK SACHS: I think that this patient's tragic story enables us to focus on one of medicine's major problems—the unwanted pregnancy. The criminal abortionist was the only source to which this young girl could turn when faced with the threat of bearing an illegitimate child. She now lies gravely ill and even if she recovers, will never be able to experience the joys of natural motherhood. The psychological harm done to this girl and her family is incalculable; the economic cost, however, is ascertainable and will run into several thousands of dollars. If one reflects on the figures presented by Dr. Freedman which indicate that over one and one-half million criminal abortions are performed in the United States each year, the problem is seen to be one of enormous magnitude. It extends far beyond unwed mothers, because the majority of abortions are performed on married women who are unable to manage an additional child for economic or psychological reasons.

I believe that it is necessary for all physicians to actively support legislation which will make it possible for any woman with an unwanted pregnancy to receive an abortion with more ease than is presently the case. Several State legislatures have passed more liberal abortion laws and the results of similar legislation enacted in the United Kingdom suggest that these laws are needed and will, in fact, significantly reduce the morbidity so well evidenced in today's case.

ADDENDUM: The patient continued to make slow progress and serial chest films showed clearing of the infiltrates. She became afebrile and her blood gases returned to normal. She was discharged from the hospital on April 9, 1970, and has been followed in the outpatient clinic.

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LAW—MEDICINE NOTES

J. Alfred Fabro, M.D.

Jacobson v. Massachusetts 25 S. Ct. 358 (1905): Compulsory Vaccination

Most physicians are not clear as to when the government can compel people to accept certain health measures, such as vaccination. Fundamental is the right of every American to control what he does with his body; nothing can be done to a person without his consent—except in certain legally justified circumstances.

This U.S. Supreme Court decision in 1905, Jacobson v. Massachusetts, established the constitutional principle providing for exceptions to this right. The Massachusetts legislature had passed this law: "The board of health of a city or town, if, in its opinion, it is necessary for the public health or safety, shall require and enforce the vaccination and revaccination of all the inhabitants thereof. . . . Whoever, being over twenty-one years of age and not under guardianship, refuses or neglects to comply with such requirement shall forfeit five dollars."

The Cambridge Board of Health in 1902 adopted a regulation requiring vaccination against smallpox. Jacobson refused. He was arrested and fined five dollars. He appealed to the U.S. Supreme Court, claiming that this regulation was in derogation of his rights secured by the Fourteenth Amendment of the U.S. Constitution providing that "No State shall make or enforce any law abridging the privileges or immunities of citizens of the United States, nor deprive any person of life, liberty, or property without due process of law, nor deny to any person within its jurisdiction the equal protection of the laws."

The Supreme Court asked: "Is this statute . . . inconsistent with the liberty which the Constitution of the United States secures to every person against deprivation by the State?"

The authority of the state to pass such a law is called the police power, which recognizes a state's authority to enact quarantine laws and "health laws of every description." The police power of the state entitles it to pass such reasonable regulations as will protect the public health and the public safety.

Jacobson insisted that his liberty was being invaded; that compulsory vaccination was unreasonable, arbitrary, and oppressive; that the law was hostile to "the inherent right of every free man to care for his own body and health in such way as to him seems best." The court disregarded his claim that the procedure was in some cases dangerous. It held that the risk of injury was too small to be seriously weighed as against the benefits coming from the discreet and proper use of the preventive.

The court stated that his rights were not absolute; that there are some restraints to which every person is necessarily subject for the common good. "Real liberty for all could not exist under the operation of a principle which recognizes the right of each individual person to use his own, whether in respect to his person or property, regardless of the injury that may be done to others.

"Persons and property are subjected to all kinds of restraints and burdens in order to secure the general comfort, health, and prosperity of the State." The court held that this regulation "was necessary for the public health or the public safety." And where the general safety of the public is concerned, every well-ordered society has the duty of conserving the safety of its members.

The legislature had passed the law on the theory that "vaccination was at least an effective, if not the best known, way in which to meet and suppress the evils of a smallpox epidemic that imperiled an entire population."

The statute was adopted for the protection of the public health and the public safety, confessedly endangered by the presence of a dangerous disease.

The issue turned on the fact that smallpox was a dangerous and communicable disease; and that the state could pass laws requiring an individual to be vaccinated to protect the public, not himself.

The court observed, however, in order to prevent misapprehension from its decision, that the police power of the State may be exerted in such circumstances so arbitrary and oppressive in particular cases as to justify the interference of the courts to prevent wrong and oppression to individuals.

This decision provides the constitutional basis for adoption by government of health measures, such as requiring vaccination against polio, where

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refusal by a person may endanger the public health. But it does not provide justification for requiring medical treatment or measures to protect the individual for his own good; or where his refusal does not endanger the public. We Americans have not yet reached the point requiring an adult to take measures for his own health where such refusal does not endanger others. Though the case was decided in 1905, it is still quoted as authority for adoption of public health laws when necessary for the common good.

Doctor's Office

E. H. S. Ahmed, M.D. announces the opening of an office for the practice of internal medicine and cardiology at 114 East Avenue, Norwalk.

Robert W. Drury, M.D. announces the opening of an office for the practice of internal medicine at 2900 Main Street, Glastonbury.

Will J. Ellzey, M.D. announces the opening of an office for the practice of internal medicine at 132 Mansfield Avenue, Willimantic.

Robert W. Ferraro, M.D. announces the opening of an office for the practice of orthopedic surgery and fractures in association with the Middlebury Orthopedic Group, Inc. at Judd Hill Road, Middlebury.

Michael A. Friedman, M.D. announces the opening of an office for the practice of dermatology at 35 Tamarack Avenue, Danbury and 144 Morgan Street, Stamford.

Anastasios B. George, M.D. announces the removal of his office to 85 Jefferson Street, Hartford, for the practice of ophthalmology.

Aziz A. Ghaussy, M.D. announces the opening of an office for the practice of internal medicine at 547 Main Street, Middletown.

Harold P. Kaplan, M.D. announces the opening of an office for the practice of internal medicine and gastroenterology in association with Internal Medicine Associates at 219 West Main St., Meriden.

Bernard Kosto, M.D. announces the opening of an office for the practice of urology at 124 Jefferson Street, Hartford.

Marvin Lewin, M.D. announces the opening of an office for the practice of urology in association with Dr. John H. Small and Dr. Philip Fleisher at 50 Ridgefield Avenue, Bridgeport.

Umberto Squattrito, M.D. announces the opening of an office for the practice of psychiatry at 85 West Street, Danbury.

John A. Willis, M.D. announces the opening of an office for the practice of general medicine at 6004 Main Street, Trumbull.

CANCER EDUCATION WEEK

As President of the Connecticut Division, American Cancer Society, I would like to alert physicians to an intensive statewide educational program to make the public more aware of the seven safeguards of cancer which will get underway on Sunday, September 27. That day will mark the beginning of Cancer Education Week, which is being sponsored by the Connecticut Division of the American Cancer Society.

Each day of the week will be devoted to one of cancer's safeguards, which are:

C hange in bowel or bladder hints
A sore that does not heal
U nusual bleeding or discharge
T hickening or lump in breast or elsewhere
I ndigestion or difficulty in swallowing
O bvious change in wart or mole
N agging cough or hoarseness

Because the physician is the number one health educator, we are asking for your support during Cancer Education Week in several ways.

Literature for the layman on cancer is available for your waiting rooms from your local Unit of the American Cancer Society. Some of you, as members of the local Unit's speakers' bureau, may be called upon to speak to local groups on the importance of early detection and treatment of cancer. Free medical education materials, such as films, the latest literature, monographs and reprints are also available from your local ACS Unit office·

The theme for this year's Cancer Education Week is "Act Today—Don't Delay! Practice Cancer's Safeguards!". In keeping with this theme, the emphasis is on education and positive action on the part of the individual to protect himself by knowing and practicing the safeguards against cancer. When one considers that nationwide over 100,000 cancer patients will probably die in 1970, who might have been saved by earlier and better treatment, it is fitting indeed to enlist the aid of every physician in the state of Connecticut to support Cancer Education Week and every week toward the aim of Saving More Lives Now.

Paul G. Kuehn, M.D., President
Connecticut Division
American Cancer Society

CORRESPONDENCE

Members of the Society are invited to communicate with the Editor of CONNECTICUT MEDICINE expressing their opinions or giving information as to any matter of interest to the members. The Editorial Board reserves to itself the right to select the communications or excerpts therefrom that will be published and to reject others. As with other material which is submitted for publication, all correspondence will be subject to the usual editing and possible abridgment. Material should be typewritten double spaced, and be of reasonable length (not over 1½-2 pages). Address all correspondence to: THE EDITOR, CONNECTICUT MEDICINE, 160 St. Ronan Street, New Haven, Connecticut 06511.

Dear Louis,

As I started reading *Connecticut Medicine,* edition for July 1970, I could not help but think what you have accomplished for the *Journal.* I have seen it grow from a nondescript publication to one of importance, and I consider that this is entirely due to you. Now that I have semi-retired, I spend quite a lot of my time reading medical journals, and I must confess that some of the articles I wade through, in such journals as the *Annals of Medicine,* and so on, only convince me that if there was some place where I could go and have six weeks of reorientation in modern medicine, it would be a good thing to do. I am inclined to think that the conditions discussed in the journals are not too far different from what you and I met twenty years ago, but the terminology has become complicated. I was very pleased to see how *Connecticut Medicine* continues to be a journal which can be useful to most doctors, with articles of interest, and yet of high scientific excellence.

These are my thoughts until I reach Page 522, with your very kind review of my last book, *Mastering Your Emotions.*

I need not tell you that an author, if I may call myself one, is very sensitive about his literary children. For many years I used to review new medical books for the *Journal of the American Psychiatric Association,* and I learned to be considerate of the authors, sometimes doing exactly what you did with my book, namely actually telling people what was in it, rather than what I thought about it.

I not only want to congratulate you on what you have accomplished with *Connecticut Medicine,* but to thank you for the review of *Mastering Your Emotions.*

I wish that you might have some common-sense psychiatrist who would write a department of what is happening in psychiatry—sometimes it might be one page, again it might be two or three. The happenings and developments I think might be interesting to all physicians, particularly if it were written with that in mind. For example, at the last Meeting of the World Psychiatric Association in London, a neurologist discussed with a psychiatrist errors which he felt the psychiatrists might be making. It was their belief that psychiatrists should stick to the factors of psychiatric medicine, rather than trying to cure the ills of the world, involving themselves in social issues to the loss of psychiatric disease. It was a valuable discussion in my opinion. The American Psychiatric Association, at its last meeting, decided to devote two years to the Study of Violence, and quite frankly I think neither they nor the Committee they appointed can be very helpful in this direction. Psychiatry is of importance to all who practice medicine, and you should have one or two pages devoted to this subject. Perhaps you might take this up with the psychiatric member of your Editorial Committee. But once again, my real purpose was to congratulate you on what the Journal has become and to thank you for your kind review.

With best regards, I am

Sincerely,
William B. Terhune, M.D.
New Canaan, Conn.

To The Editor

Emergency Admission in Hospital Utilization

UTILIZATION REVIEW of hospital patients includes a determination of the propriety of emergency admissions. Large hospital emergency rooms may have a holding area where hospitalization necessity can be determined by a 3 to 12 hour work-up. In small hospitals where decisions have to be made quickly, all admitting physicians should be expected to use the same criteria for admission. Science depends on measurement and if abstractions are converted to numerical entities, judgment without subjective quality is possible. A quantifying method which attains uniformity as well as objectivity is submitted.

The evaluation method is shown in the table, and is usable by the admitting and reviewing physician as well. Numerical values are assigned to each of seven categories, an emergency admission is considered justified by an agreed numerical total. This is a more practical means of achieving objectivity than seeking outside committees of physicians. The admitting physician fills out the evaluation sheet for each admission and makes his estimates when the history is dictated. The reviewing team need only judge on the propriety of his evaluations in accordance with the available data.

As to prognosis, the six and five values are self-explanatory. Four is a matter of judgment, but differences in judgment are limited to a small area. Three also requires supportive data to make the judgment acceptable. Two and one indicate unknown illness, the value acknowledges that young have greater recoverability.

Under diagnosis, four requires no explanation, three is definable and leaves only a small area for possible difference of opinion between the admitting physician and the reviewing physician. Two and one require supportive data. The category "psychoneurotic" recognizes that mental and emotional factors may make it necessary to remove the patient from the home. The category, family and social, indicates other marginal factors that generate the occasional necessity of providing skilled, dependable nursing care and observation, instead of what can be given by the family at home. Police and public relations may be complex but only three judgments are made and these are all obvious. The administrative and economic factor cannot be ignored in hospital management, variations of supply and demand in hospital space must be recognized in utilization.

Time of day suggests that more may be expected of a doctor during the day to care for a patient away from the hospital. What a physician has to do, explain and be responsible for demands more of him in the care of a patient away from the hospital. Since most physicians who are available at night also have a full working day ahead of them, it is realistic to be more lenient at night and allow him to conserve effort in night work when he has been gotten out of bed.

Sidney Vernon, M.D.
Willimantic, Conn.

SCORE GUIDE FOR EMERGENCY ADMISSION

POINTS		EVALUATION
PROGNOSIS		
6	CLINICAL SIGNS SUGGEST THAT DEATH IS CERTAIN IF IMMEDIATE TREATMENT IS NOT GIVEN; ACUTE CARDIOVASCULAR DISEASE, OR OXYGEN LACK.	
5	SEVERE PAIN is present, POTENT ANALGESICS are necessary, and severe disease is obvious.	
4	DETERIORATION is EXPECTED if not hospital-treated, diagnosis may be unknown.	☐
3	Severely ill, diagnosis unclear	
2	Hospital care is necessary, elderly person with uncertain prognosis.	
1	A younger person with unclear outcome.	
DIAGNOSIS		
4	THE DIAGNOSIS IS OF AN OBVIOUSLY FATAL DISEASE WITH SUPPORTIVE CARE NEEDED	
3	CHRONIC DISEASE RECENTLY AGGRAVATED, and relief is essential.	
2	The diagnostic need is URGENT.	
1	The condition is diagnosed but FURTHER EVALUATION is necessary.	☐

PSYCHONEUROTIC

2 There is an obvious PSYCHIATRIC EMERGENCY.
1 The family is HYSTERICAL.
0 No problem. ☐

FAMILY AND SOCIAL

1 Family are obviously INCAPABLE OF CARING FOR THE PATIENT AT HOME because of ignorance, or social or emotional factors.
½ A LANGUAGE DIFFICULTY makes diagnosis difficult or impossible because information cannot be obtained. ☐
0 No problem.

POLICE AND PUBLIC RELATIONS

1 Brought to the Emergency Room by AMBULANCE, or by POLICE or by a disinterested party fearful of the outcome.
½ Brought in by friends who found the patient ill. ☐
0 No problem.

ADMINISTRATIVE, ECONOMIC

1 Hospital occupancy is lower than the break-even point of overhead costs.
½ There are plenty of beds. ☐
0 If the occupancy in the hospital is high.

TIME OF DAY

1 The problem occurs between 11:00 p.m. and 5:30 a.m.
½ The patient appears in the Emergency Room between 7:00 and 11:00 at night or between 5:30 and 8:30 in the morning. ☐
0 Patient appears during the day.

Total Points,
(Admissibility Index) ☐

PLEASE MARK YOUR CALENDAR

179th CSMS ANNUAL MEETING

TO BE HELD AT THE

HARTFORD HILTON HOTEL, HARTFORD

APRIL 27, 28, 29, 1971

PLAN NOW AND SAVE THE DATES

From the

Connecticut Regional Medical Program

On July 30, 1970, the Connecticut Regional Medical Program sent to Washington a Request for a Supplemental Grant totaling $1,635,000 to cover the costs of operation of eight programs during 1971-73. Copies of the Request are available to Connecticut State Medical Society members through CRMP Headquarters, 272 George St., New Haven.

The official transmission contains the following statement by Mr. Arthur M. Rogers, Chairman of the CRMP Advisory Board, as a part of a letter of transmittal to Harold Margulies, M.D., Acting Director of the national Regional Medical Programs Service:

"It is pertinent to describe briefly the steps in the development and processing of a grant proposal in Connecticut before it is sent to the Regional Medical Programs Service.

"As background, the official organizational structure of CRMP contains four 'Conferences' which are advisory to the Advisory Board. Each of these Conferences elects one member to the Board. These Conferences are made up of: (a) the presidents of the boards of trustees of the hospitals of Connecticut, some 50 in number; (b) the chiefs of staff of those hospitals; (c) the administrators of those hospitals; and (d) official representatives of some 60 state-wide health and health-related agencies which are active on the Connecticut scene. Two of these Conferences meet monthly with CRMP staff and the others quarterly. All Conference members receive the weekly *CRMP Newsletter* and selected other CRMP materials, including key submissions to Washington. Accordingly, a large number of health leaders in Connecticut have a continuing opportunity to be well informed about CRMP.

"A typical request to CRMP for financial support for a program activity starts with a conversation between a member of one of the Conferences and a staff member of CRMP. Discussions then move to the organizational setting of the Conference member and involve appropriate staff members there. Since most CRMP-supported activities promote new or expanded relationships among health organizations to achieve a common goal, the discussions expand to include representatives of the related organizations or agencies. Thus CRMP staff have a considerable opportunity to advise on the form and content of a developing proposal.

"Applicant agencies are told that their requests will be measured against certain criteria which have been established by the CRMP Advisory Board. These are as follows: (a) the proposed program must be scientifically sound; (b) the proposed program should contribute in a significant way toward implementing the grant strategy of CRMP, which seeks to promote the best possible medical care to all 3,000,000 citizens of Connecticut in the most efficient way; (c) it should focus on an important health problem of local or regional significance and should present a practical approach to the study and/or resolution of the problem; (d) it should have the potential for duplication in or extension to other parts of Connecticut; (e) there should be evidence of a capacity for early implementation with full approval of the authoritative body of the applicant agency evident and responsible leadership for the program identified; (f) any matching money or resources available to undertake the activity should be documented; (g) the length of financial support needed from CRMP should be discussed as well as future plans for take-over, placing on a self-supporting basis or phasing out; (h) where appropriate, a technical advisory committee jointly selected by the applicant agency and CRMP should be projected to encourage regional acceptance of the program and to provide counsel and advice in implementation.

"Once the program proposal has been submitted to CRMP staff, it is then taken to the CRMP Review and Evaluation Committee for critical appraisal. The R&E Committee is a body of 16 distinguished Connecticut citizens who have been appointed by the Advisory Board to examine program proposals in depth prior to their submission to the CRMP Executive Committee and Advisory Board. This examination consists of full Committee discussion, led by primary and secondary reviewers, and it often includes a site visit. The judgments of the R&E Committee are referred back to the applicant. This often leads to the submission of supplemental data and occasionally to a revision or a withdrawal of a proposal.

"When the R&E Committee has completed its review of a program proposal it transmits a written report to the Executive Committee, giving its views of the strengths and weaknesses of the proposal and its recommendation for action.

"The Executive Committee then considers the proposal and takes appropriate action—one possible action being to recommend the proposal to the Advisory Board for submission to Washington. The Advisory Board then takes the final action so far as Connecticut is concerned. (The Advisory Board is the governing body of CRMP by delegation from Yale University, which is the grantee agency).

"In the development of the current Request for a Supplemental Grant, the CRMP Review and Evaluation Committee held meetings on May 19, June 9, June 30 and July 9, each lasting about six hours. In addition, site visits were conducted by teams of R&E Committee members and selected consultants on five of the proposals. The Executive Committee met on May 25, June 9 and July 13, for about four hours each with the last meeting being devoted almost entirely to the proposals in this request. Finally, the Advisory Board met on July 16 and gave its approval, with certain qualifications, to the recommendations before it."

Placement Wanted

ANESTHESIOLOGY—37 years of age, Eligible, presently in practice, wishes solo, associate or group type practice in Connecticut. With Connecticut license. Available immediately.

ANESTHESIOLOGY — 45 years of age, Eligible with National Boards, wishes group, associate, institutional or industrial type practice in Connecticut. Available immediately.

FAMILY PRACTICE—55 years of age, Certified with National Boards, wishes group or institutional type practice in Connecticut. Available immediately.

GENERAL PRACTICE—30 years of age, wishes solo, associate or institutional type practice in a small community in Connecticut. Military obligation completed.

INTERNIST — ENDOCRINOLOGY — 33 years of age, Eligible with National Boards. Prefers to practice internal medicine-endocrinology in a group or with associate, but must affiliate with university-type teaching hospital. Military obligation completed. Available immediately.

INTERNIST—33 years of age, Eligible with National Boards, wishes group or associate type practice in Connecticut. Available in October.

INTERNIST—36 years of age, Certified with National Boards, wishes group or associate type practice in Connecticut. Available in August.

INTERNIST—46 years of age, Certified with National Boards, wishes group, institutional or industrial type practice in Connecticut. Presently in practice. Connecticut license. Available immediately.

INTERNIST—36 years of age, Eligible with National Boards, presently in practice wishes solo type practice in Connecticut. Available in the fall.

INTERNIST—34 years of age, Eligible, wishes associate or institutional type practice in Connecticut. Presently in practice.

NEUROSURGERY—32 years of age, Eligible with National Boards, wishes solo or associate type practice in Connecticut.

OBSTETRICS & GYNECOLOGY—33 years of age, Eligible with National Boards, wishes group type practice in a medium size community in Connecticut. Presently in practice. Military obligation completed. Contact: Stephen B. Berkowitz, M.D., 415 Grand Street, Apt. 1801, New York, New York 10002.

OPHTHALMOLOGIST—31 years of age, Certified with National Boards, wishes solo, group or associate type practice in Connecticut. Available immediately.

PATHOLOGIST—31 years of age, Certified with National Boards, wishes group, associate or institutional type practice in a large or medium size community in Connecticut. Available immediately.

PEDIATRICIAN—33 years of age, Certified, wishes solo, group, associate or institutional type practice in a large or medium size community. Academically oriented practice prefer medical school affiliation. Available immediately.

PEDIATRICIAN—40 years of age, Eligible, wishes solo, group or associate type practice in a medium or small size community in Connecticut. Available immediately. Contact: Vasant G. Yadav, M.D., 201 W. Cuthbert Blvd., Oaklyn, New Jersey 08107.

PEDIATRICIAN—35 years of age, Certified, wishes group, associate or institutional type practice in Connecticut. Available immediately.

THORACIC AND CARDIOVASCULAR SURGERY—36 years of age, presently in practice, wishes group or associate type practice in a large community in Connecticut. Primarily interested in thoracic and cardiovascular surgery but would be interested in combining this with general surgery. Available immediately.

ANYONE INTERESTED IN THE ABOVE IS ASKED TO CONTACT THE PHYSICIANS PLACEMENT SERVICE, 160 ST. RONAN ST., NEW HAVEN, CONNECTICUT 06511.

Placement Opportunities

FAMILY PRACTICE—Third man for Family Practice, no investment, salary if desired, equal time off, new 120-bed hospital next to office, Northern Connecticut, 15 miles from Hartford. J. Kristan and L. O'Connor, M.D., 57 Union Street, Rockville, Connecticut 06066.

OPENING FOR INTERNIST in 496 bed State Veterans Hospital—$21,911-$26,729—plus 6% adjustment October 1970. Many fringe benefits. Write or call Personnel Officer, Veterans Home and Hospital, Rocky Hill, Connecticut, 529-2571, Extension 395.

OBSTETRICS & GYNECOLOGIST—Third man needed, board-eligible or certified, with military obligations completed, to join two other physicians in Middletown. Starting salary $18,000; partnership after three years. Congenial staff, University town. Prospective applicants are encouraged to write to Donald E. Miller, M.D., 18 Crescent Street, Middletown, Connecticut.

OFFICE-HOUSE for sale. Connecticut shoreline area. Seven room office fully equipped—x-ray and lab. Excellent opportunity for immediate income from active, lucrative, practice. Close proximity to Yale-New Haven Medical Center. Physician recently deceased. For details write to: P.O. Box 222, Clinton, Connecticut 06413.

PATHOLOGIST—part time for the Masonic Home and Hospital, Wallingford, Connecticut. Attractive, well paying, steady and not much time consuming position.

PATHOLOGIST ASSISTANT—Board qualified or eligible. Attractive newly established position available in a progressive 320 bed accredited general hospital located in beautiful Southern Connecticut. Clinical and anatomic pathology. Expanding hospital laboratory with approved school of medical technology. Salary open, excellent benefits. Please send curriculum vitae to: Gilles Allard, M.D., Pathologist, Director of Laboratories, St. Joseph's Hospital, Stamford, Connecticut 06904.

PEDIATRICIANS—Two Pediatricians are needed to serve a growing community of over 50,000 people. Area consists of several small towns with population of 3,000 to 14,000 each. Good country living with easy access to larger cities via well developed highway system. Community hospital is now expanding and more physicians are needed. Contact: E. B. Raheb, Chief of OB & GYN, Day Kimball Hospital, Putnam, Connecticut 06260.

PEDIATRICIANS—At least two pediatricians are needed for private practice to serve a growing community of over 50,000. Area consists of several towns with 3,000 to 14,000 population each. Good country living with easy access to major cities via well developed highway system. Contact: Edmond B. Raheb, M.D., Chief of OB-GYN, Day Kimball Hospital, Putnam, Connecticut. (203) 774-5151.

PHYSICIANS AND RESIDENT PHYSICIANS—opportunities with the State of Connecticut in medical hospitals, institutions for the mentally retarded, and Veterans' Home and Hospital. Residencies $10,694-$16,110; Physician $17,760-$21,960; Senior Physician $19,303-$23,755; Maternal and Child Health Physician $21,002-$25,700; Medical Consultant $21,002-$25,700; Internist $21,911-$26,729; Chief, Epidemiology Section $21,911-$26,729. Excellent benefits. For further information contact Mr. John Crowley, Agency Personnel Administrator, Department of Health, 79 Elm St., Hartford, Connecticut or Mr. Edmund Buetsch, Personnel Officer, Veterans' Home and Hospital, Rocky Hill, Conn.

PHYSICIAN—part time; to work mornings in the office only. Practice limited to general medicine and aviation medicine. For further information contact, James E. Crane, M.D., 965 Hope Street, Stamford, Connecticut.

CONNECTICUT-SENIOR PSYCHIATRISTS—In a 3 year accredited dynamic, decentralized community-oriented mental hospital. Affiliated with Yale University, Wesleyan University, and University of Connecticut. Excellent opportunities for professional growth and advancement. Starting salary range $19,303-$26,986, depending on experience and training. Liberal benefits. Eligibility for Connecticut license required. Send all particulars in first letter, including references to Mehadin K. Arafeh, M.D., Superintendent, Connecticut Valley Hospital, Box 351, Middletown, Connecticut 06457.

PSYCHIATRISTS AND PSYCHIATRIC RESIDENTS—Openings in the mental hospitals and mental health clinics of the State of Connecticut. Residencies, $10,694-$16,110; Psychiatrist I, $19,303-$23,755; Psychiatrist II, $20,128-$24,700; Psychiatrist III, $21,911-$26,729. Excellent benefits and opportunity for advancement. For further information contact Mr. Robert Tacey, Agency Personnel Administrator, Department of Mental Health, 90 Washington Street, Hartford, Connecticut.

PSYCHIATRIC RESIDENT, PHYSICIANS, PSYCHIATRISTS—positions available at Norwich Hospital. Community oriented, geographically unitized hospital with many forward-looking, exciting programs. Fully approved for three years psychiatric residency training with NIMH grants available. Resident's salaries begin at $10,690 and all salaries will be increased by 6% in October, 1970. Many fringe benefits. Write Superintendent, Norwich Hospital, Norwich, Connecticut 06360.

The Connecticut State Medical Society offers placement assistance through the Physician Placement Service, 160 St. Ronan Street, New Haven, Connecticut, 06511. This service is for the use of physicians seeking locations as well as physicians seeking associates, and is without charge.

ANYONE INTERESTED IN ASSISTANCE THROUGH THE PHYSICIANS PLACEMENT SERVICE IS ASKED TO CONTACT THE EXECUTIVE DIRECTOR'S OFFICE, 160 ST. RONAN STREET, NEW HAVEN, CONNECTICUT 06511.

Suppression Of Autoimmune Disease In NZB And (NZBXNZW F) Hybrid Mice By Infection With Malaria

(*Nature*: 226, 266, April 18, 1970) Infection of malaria enables mice to maintain tolerance to an antigen possibly of viral origin which usually induces a harmful immune response.

Considerable caution is needed in extrapolating the results of these experiments by consideration of human disease. They do, however, support the idea that repeated parasitic infections may have some protective action against the development of autoimmune disease in man.

Elucidation of the mechanism by which infection with malaria suppresses autoimmune disease in mice might indicate a new approach to the treatment of human autoimmune disease.—L.H.N.

In Memoriam

Antupit, Louis, Jefferson Medical School, 1923. Dr. Antupit was a surgeon in the Hartford area since 1929. An Army veteran of World War I, he was senior attending in surgery at Mt. Sinai Hospital. He was also a member of the staff at St. Francis Hospital, and a member of the courtesy staff at Hartford Hospital. Dr. Antupit was a member of the Hartford County Medical Society, the Connecticut State Medical Society, and the American Medical Association. He was also a fellow of the American College of Physicians and Surgeons. Dr. Antupit died August 1, 1970 at the age of 73.

Dinan, Henry Philip, Tufts Medical School, 1938. Dr. Dinan was a private practitioner in the Stratford area since 1943. In 1958 he was appointed acting city health director and was named permanent health director in 1959. Dr. Dinan was administrator of Bridgeport's Office of Humane Affairs since 1962 and medical director of Hillside Hospital, and served as a consultant at Bridgeport and St. Vincent's hospitals. He was a member of the Connecticut State Medical Society and the American Medical Association, and was active in the American Thoracic and American Geriatric associations. Dr. Dinan died July 24, 1970 at the age of 57.

Weise, Ellwood C., Sr., Jefferson Medical School, 1920. Dr. Weise was a dermatologist in the Bridgeport area since 1920. He was consulting dermatologist in the department of medicine, section of dermatology, and former attending dermatologist and chief of the clinical division of dermatology of Bridgeport Hospital. He had also served as former assistant attending dermatologist at the Vanderbilt clinic, Columbia Presbyterian Medical Center, New York City, as associate dermatologist at St. Vincent's Hospital, and attending dermatologist at the City of Bridgeport dispensary. Dr. Weise was one of the founders of the section on Dermatology of the State Medical Society and was also a diplomat of the American Board of Dermatology. He was president of the Bridgeport Medical Association in 1941 and was elected president of the Connecticut State Medical Society in 1958, and also served as a Society delegate to the American Medical Association from 1962-68. In 1968 he received a special service award from the Society. Dr. Weise died July 18, 1970, at the age of 74.

MEETING NOTICES

The information on this "notices" page is offered as a service to all specialty groups and allied health agencies in order to publicize postgraduate educational opportunities available to subscribers. The deadline for publication in Connecticut Medicine is the tenth of the preceding month, i.e., the tenth of September for the October issue. Send copy to: Connecticut State Medical Society, 160 St. Ronan Street, New Haven, Connecticut 06511.

September 23—Wednesday
Connecticut Nurses' Association and Connecticut League of Nursing
Forum on Nursing Education
St. Francis Hospital, School of Nursing, DeSalles Hall, 338 Asylum Street, Hartford, Connecticut—8:30 A.M. to 4:00 P.M.
Registration and luncheon: $5.00 for members; $10.00 for non-members.

September 25-26—Friday and Saturday
Postgraduate Course for Pediatricians
"Disorders of the Spleen in Childhood"
Yale University School of Medicine, Department of Pediatrics
Speakers: Drs. Howard Pearson, Lawrence Pickett, Norman Talner and Joseph Bertino.
Contact: T. F. Dolan, Jr., M.D., Department of Pediatrics, Yale University School of Medicine, New Haven, Connecticut 06510. (Telephone 203-436-8388)

September 29—Tuesday
Lecture: "Psychiatry in Public Mental Hospitals"
Connecticut Valley Hospital, Merritt Hall Auditorium, Middletown, Connecticut—10:30 A.M.
Speaker: Oscar K. Diamond, M.D.

September 30—Wednesday
Connecticut Nurses' Association
"Three Aspects of Disaster Nursing"
Valle's Steak House, Hartford, Connecticut
8:00 A.M.-4:00 P.M.
Speakers: David Belise, Assistant Administrator at McLean Hospital, Boston. Edward McGinnis, Assistant Professor of Psychiatric Nursing, University of Bridgeport. Mary Anna Moore, Assistant Director of Nursing Program, American Red Cross.
Registration and luncheon: $4.00 for members; $9.00 for non-members.

October 5—Monday
Lecture: Problems of Abortion
Hartford County Medical Association—8:00 P.M.
230 Scarborough Street, Hartford, Connecticut
Speaker: Keith P. Russell, M.D., Clinical Professor of OB & GYN, U.S.L.A.
This lecture will be part of the "Ladies Night" program. Physicians, their wives and guests are welcome.

October 5-9—Monday-Friday
The American Academy of Ophthalmology and Otolaryngology
International Hotel, Las Vegas, Nevada
Contact: C. M. Kos, M.D., 15 Second Street, SW, Rochester, Minnesota 55901

October 7—Wednesday
Lecture: "Twin Studies: Genetic, Constitutional, Biochemical Factors and Schizophrenia"
Connecticut Valley Hospital, Merritt Hall Auditorium, Middletown, Connecticut. 10:30 A.M.
Speaker: James R. Stabenau, M.D.

October 12-16—Monday-Friday
The American College of Physicians
Course in Interviewing, Data Gathering and Record Systems for the 1970's
Michigan State University College of Human Medicine, East Lansing, Michigan
Contact: A.C.P., 4200 Pine Street, Philadelphia, Pennsylvania 19104

October 14—Wednesday
Connecticut Nurses' Association
"The Nurses's Role in the Drug Scene"
V. A. Hospital, West Spring Street, West Haven, Connecticut
Speakers: Donald Pet, M.D., Chief of Professional Services of the Alcohol and Drug Dependence Division, State Department of Mental Health. Jack Cohn, former addict. Helen McClafferty, R.N.

October 17-21—Saturday-Wednesday
American Society of Anesthesiologists
American Hotel, New York City
Contact: John W. Andes, 515 Busse Highway, Park Ridge, Illinois 60068

October 19—Monday
Lecture: "Changing Concepts of Psychosomatic Medicine"
Connecticut Valley Hospital, Merritt Hall Auditorium, Middletown, Connecticut. 10:30 A.M.
Speaker: Morton F. Reiser, M.D., Chairman of the Department of Psychiatry at Yale School of Medicine.

October 20-23—Tuesday-Friday
The American College of Physicians
Course on the Neurological Aspects of Internal Medicine
Duke University Medical Center, Durham, North Carolina
Contact: A.C.P., 4200 Pine Street, Philadelphia, Pennsylvania 19104

November 18—Wednesday
Perinatal Seminar
Mary S. Harkness Auditorium, Yale Medical School
Speakers will include: Dr. Alex Minkowski, Director of the Center de Recherches Biologiques Neonatales, Paris, France. Two discussions:
"The Biochemistry of the Small for Dates Infant"
"The Pediatrician and the Problem of High Risk Pregnancies"
Richard Banfield, M.D., and Ruth Wilf, Ph.D.—Discussion on various aspects of a prepared child birth program.
Panel Discussion on Neonatal Intensive Care and Transitional Care of the New Born Infant:
Moderator: Robert H. Usher, M.D., Neonatal Unit and Royal Victoria Hospital, Montreal, Quebec, Canada.
Alexander Campbell, M.D., Assistant Professor of Pediatrics and Director of the Neonatal Unit at Yale University School of Medicine.
Stanley James, M.D., Columbia University College of Medicine.
Jeryl Gagliardi, R.N., New Born Intensive Care Unit, Yale New Haven, Hospital.
Contact: Robert L. Harris, M.D., 581 Farmington Avenue, Hartford, Connecticut. (Telephone 203-232-5202)

November 29-December 2—Sunday-Wednesday
Clinical Convention
American Medical Association
Boston, Massachusetts

April 27, 28, 29, 1971—
Tuesday, Wednesday, Thursday
179th Annual Meeting
Connecticut State Medical Society
Hartford Hilton Hotel, Hartford, Connecticut

Science News

Appalachian Program: A Mechanism For A National Growth Policy

(*Science*: 169, 32, July 3, 1970, Carter, K. H.) More than 1 billion in special aid funds have been given to the 13 Appalachian states by an act of Congress in 1965. Over half has gone into highways, but substantial sums have been spent on vocational schools, health facilities, and other needs. However, the program has been slow to reach the legions of poor, illiterate, and unskilled.

In the effect to create a self-sustaining economy to afford good jobs and keep the ablest and most mobile elements of the population from leaving Appalachia, the goal is far from being attained. The economy is still very sick, and has to be kept alive by massive transfusions of federal money.

The Appalachian Regional Commission (ARC) with an annual budget of 300 million has not yet dealt with two fundamental problems of its own region, the evident need for tighter control of "strip mining" which is ruining the country-side and for a "severance" or production tax on coal. The ARC behaves as though it remains subservient to outside economic interests instead of working to develop publicly owned hydropower systems and mine-mouth power systems. This presumably because electric utilities, railroads and other corporate interests are opposed.

Up to now ARC has not reached these two gut issues which cannot be avoided much longer without leaving it open to charges of shameless dereliction of duty.—L.H.N.

AMA Abortion Stand

(*Science*: 169, 34, July 3, 1970) The AMA has voted for the first time in its 123-year history to consider abortion a "medical procedure" and to allow doctors to perform abortions for social and economic reasons as well as medical.

The new policy calls for consultation by two physicians other than the patient's doctor and for performance of the operation in an accredited hospital by a licensed physician. No doctor or hospital should be compelled to perform abortions, the AMA said.

The president of the 6000-member National Federation of Catholic Physicians Guild has called upon Catholic doctors to resign from the AMA in protest against the new policy.

One consequence of the liberalized abortion laws in the State of New York is the resignation of Dr. R. R. Onorata as Director of Obstetrics and Gynecology at Yonkers Hospital in New York. The law conflicted with the doctor's views as a Roman Catholic which rendered it impossible for him to make decisions on abortions.—L.H.N.

Black Doctors

(*Science*: 169, 34, July 3, 1970) Meharry Medical College has received a $1-million grant from the Alfred P. Sloan Foundation of New York. The grant will be used to increase the number of full-time faculty members over the next decade so that the college may triple its student enrollment, currently 500.

Meharry is the only predominantly black private medical college in the United States. It has graduated about half of the black physicians and dentists now practicing.—L.H.N.

Human Suffering In Vietnam

(*Science*: 169, 6, July 3, 1970, Haseltine, W., Carter, W. R., Long, N. V.) When evaluating the effects of the massive application of herbicides in Vietnam is: what are the health hazards to the exposed people, what is the impact on their lives, what are the long-range effects on the Vietnamese society, and finally, what is the effect on the ecology.

The Department of Defense has acknowledged that they have laid waste to one half a million acres, or about 10 per cent of the arable land. But neutral estimates give a much higher figure. The impact of this deliberate spraying on the Vietnamese society is enormous. People are forced to abandon their ruined fields and seek food in so-called "refugee camps" and cities. Saigon itself has grown from 250,000 to 3 million.

The defoliation problem is purposefully directed against the rural population of South Vietnam and it's geared to move people to refugee camps. People from the country-side are being uprooted and driven into the cities and refugee camps where they can be controlled.

We are producing not merely the deliberate destruction of the environment, but also the deliberate destruction of a society.

The AAAS should call for cessation of the use of the herbicides, 2,4-d and 2,4,5-T, include all herbicides in war and to form a committee to press for this end.—L.H.N.

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Organization and Functions of a Department of Internal Medicine in Community Hospitals*

(The Bulletin, 281, June 1970)

The primary purpose of the medical department of the community hospital is medical care and service to the community. Nevertheless, medical care and medical education are interdependent, a concept which is a basic feature of the organization of the medical staff and of the function of the medical service.

A. *Departmental Organization.*

1. *The Chairman of the medical service* should be known for his integrity, professional ability and willingness to serve as an example. He should be approved by the medical staff, and by appropriate officials of a medical school if the hospital is affiliated, prior to his appointment by the Board of Trustees of the hospital. However he is chosen, he should be certified by the American Board of Internal Medicine and it is desirable that he be a Fellow of the American College of Physicians. He should be able to evaluate and direct the general practice of Internal Medicine in the hospital. Though subject to annual review, his tenure of service should not be less than three years.

2. *Membership of the Medical Service.* Each member of the staff must be willing to make his patients available for teaching of undergraduate and graduate personnel. Occasional exceptions may be made to the mutual advantage of everyone concerned. The member of the teaching staff must take part in rounds, discussions, formal presentations and departmental and staff meetings. His practice must be confined to Internal Medicine and he should be certified or Board eligible. Preferably he should be a member of the American College of Physicians. There may be a member of the hospital staff who, for various reasons, does not desire to take part in the medical education program. This should be an exception.

Relief from such responsibility will reduce his exposure to the house staff, medical students, and graduate medical education activities. These activities are a privilege. The avoidance of such a privilege results in an educational loss to the nonparticipating staff member.

In his position on the teaching staff of the community hospital the volunteer or part-time teacher can serve as an attractive example of high quality medical care on a private basis. His special skills may also demonstrate to the young trainee in medicine and other staff members the results which can be obtained by providing such high quality care, and the contributions this offers to the health interests of the community.

All members of the medical service should be urged to take part in the educational activities and be expected to attend regularly scheduled departmental meetings.

B. *Facilities.*

Hospital administrators and Boards of Trustees must be made aware of the generous return from investments in facilities that improve the standard of education and practice of medicine within the hospital.

1. *Meeting and classroom space* suitably equipped.

2. *Library* facilities available containing adequate texts and periodicals, and other materials for self-learning.

3. *Appropriate clinical facilities and services* should be developed or shared according to the needs of the community.

C. *Functions of the Medical Service of the Community Hospital.*

1. *Patient Care.*

This is the primary function of the community hospital. Simultaneously with the provision of high grade medical care, medical education is made available to practitioners of medicine on the hospital staff, undergraduate students, house staff, nurses, and all allied health professionals. Although medical care is primary, it also includes medical education. This must be emphasized in the community hospital whether or not it is affiliated with a medical school.

2. *Evaluation of the medical service.*

a. Adequate recording of the professional work, and its availability for review via an *efficient medical records facility* is important to the whole hospital staff. Accuracy and completeness are essential. Excellence of the records will become a point of commendation and pride among members of the staff.

b. The *medical audit* and *peer review* provide an objective evaluation of patient care and serve as a foundation for the educational program.

3. *Control of the quality of medical care.*

This is accomplished through organized medical service meetings, maintenance of good medical records and close cooperation between the head of the department, chief of staff, and the hospital administration.

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* As suggested by the American College of Physicians' Committee on Hospitals.

4. *Privileges and discipline of staff members.*

This is an individualized problem depending on the standards of the community and the special ability of the individual. Requirements for consultation and the privilege of participation in special areas such as the coronary care unit are the responsibility of the chief of service.

5. *Residency program.*

Whether or not there is an approved residency program in the hospital, patient care is improved by following carefully the guidelines set for residency training programs, and a medical residency should satisfy the standards as set forth in the *Guide for Residency Programs in Internal Medicine,* as formulated by the Residency Review Committee in Internal Medicine of the AMA, and the *Essentials of Approved Residencies* prepared by the AMA. Copies are available on request.

Summary

The Department of Internal Medicine should be organized to provide the best possible care for the patient. It should also supply, by proper organization tailored to fit the community hospital involved, a real contribution to regional health care, including education of medical personnel and the public.

The community hospital has a unique capacity for the provision of medical care, education and clinical research.

Electrocardiographic Left Ventricular Hypertrophy And Risk Of Coronary Heart Disease—The Framingham Study

(*Ann. Intern. Med.* 72, 813, June 1970, Kannel, W. B., et al) Persons who acquired definite LVH-ECG had a residual three-fold increased risk of clinically overt coronory heart disease after adjustment for the effect of coexisting hypertension.

Possible ECG-LVH was associated with a two-fold increased risk, but this was virtually obliterated by adjustment for hypertension.

Risk of every clinical manifestation of coronary heart disease and of death in particular, was increased and 40% with prior LVH-ECG died in their initial attack, a fatality rate comparable with that of persons with prior overt coronary heart disease. ECG-LVH is thus a grave prognastic sign and a harbinger of clinically overt coronory heart disease.—L.H.N.

A Review Of Aortic Valve Homografts Over A Six And One-Half Year Period

(*Ann. Surg.*, 170, 483, 1969, Barrett-Bayer, B. G., Roche, H. H.) These authors replaced aortic valves by a homograft in 599 patients. Many were in 7th and 8th decades. Hospital mortality was 9.8 per cent and late mortality 12.7 per cent. Only 4.4 per cent of late deaths were due to valve failure. Cusp rupture occurred in 6 per cent of chemically sterilized valves. If the valves were not treated chemically there were no cusp ruptures or calcification.

Thus a homograft valve can be inserted with no greater mortality than prothetic devices. Anticoagulants are not required and incompetence is rare. —L.H.N.

Physiological Responses Of Infant Rats To Separation From Their Mothers

(*Science*: 168, 873, May 15, 1970, Hofer, Myron A.) Decreases of 40 percent in cardiac and respiratory rates occur during the first 12-16 hours after 2-week-old rat pups are separated from their mothers.

These rates decrease without significant alteration in activity level and despite maintenance of body temperature, of nutrition by intubation, of an intact litter, and of the home cage nest. What it is that elicits this response is unknown.

Such factors as olfactory and tactile stimulation provided by the mother's attention to the pups, the consummatory experience of suckling and receiving milk. Possibility of a maternal hormonal factor transmitted in rat mother's milk, must be considered.

Then the frequency, route, amount, and composition of nutrient may be crucial. The rat mother normally provides some milk every hour, and at this age daily weight gains of 2 g are common in contrast to the 1-g weight gain achieved by the five tube feedings over 24 hours.—L.H.N.

Arsenic In Detergents: Possible Danger And Pollution Hazard

(*Science*: 168, 389, April 17, 1970) Arsenic at a concentration of 10-70 ppm has been detected in several common presoaks and household detergents.

Arsenic values of 2-8 pp have been measured in the Kansas River. These concentrations are close to the amount (10 parts per billion) recommended by the United States Public Health Service as a drinking-water standard.

Waste water of these detergents can easily enter the water system and therefore contribute to water pollution.—L.H.N.

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Index to Advertisers

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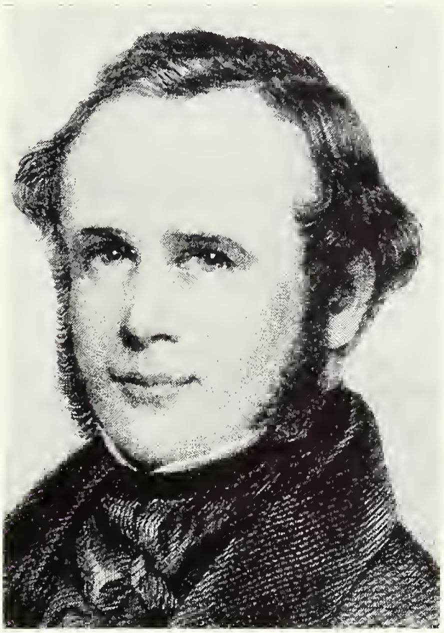

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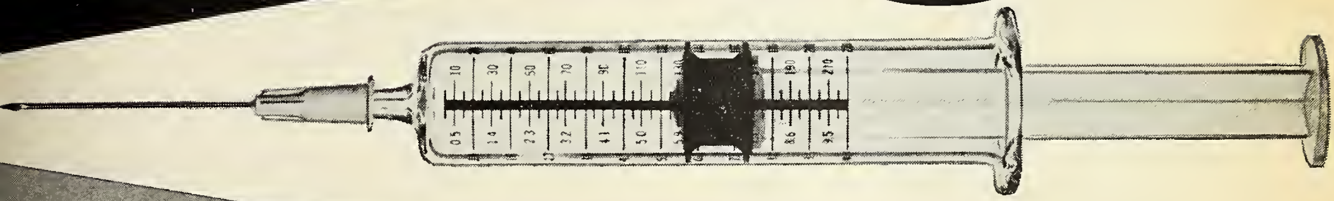

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CONTENTS

editorials

Sleep: A New Bridge Between Psyche And Soma 669
Prevention Of Cancer 670
The Illusive Herpes Virus And Its Multifarious Clinical Expressions 675
Report Of The Council On Environmental Quality Facts and Recommendations 677
Gram Negative Septicemia 679
Prediction From College Grades 683
Tracking The Y Chromosome 684
Fetal Goiter Due To Iodide Ingestion By The Mothers . . 685
The Government Downgrades Cancer Research 685
Vitamin E. Deficiency 688

scientific

Foreword, *Frederick W. Hehre, M.D., Guest Editor* 693
Dr. Horace Wells, *Stevens J. Martin, M.D.* 694
Newer Thoughts On Obstetric Anesthesia, *Robert Hook, M.D.* 696
The First Sixty Minutes Of Life, *Leandro Cordero, Jr., M.D.* 701
Interactions Between Certain Drugs Used Preoperatively and Anesthetic Agents, *John C. Daniels, M.D.* 708
Professional Liability Of Anesthesiologist, *Frank A. Manthey, M.D. and William R. Murphy* 714
Respiratory Intensive Care, *James I. Gilman, M.D.* 719
Muscle Relaxants And Some Problems With Their Use, *B. Barry Greenhouse, M.D.* 723

departments

The President's Page 727
From The Executive Director's Office 728
Physician's Placement Service 732
Electrocardiogram-Of-The Month, *Hyman M. Chernoff, M.D.* 740
Correspondence
A Comment On Town Gown Rivalry 742
Library Facilities 745
Woman's Auxiliary 745
Around The State 748

miscellaneous

Anesthesiology Ground Rounds—Yale-New Haven Hospital, *Samuel M. Lerner, M.D. and Frederick W. Hehre, M.D.* 735
Connecticut Regional Medical Program 745
Science News 752
Meeting Notices 754

Connecticut Medicine

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Editorials

Sleep: A New Bridge Between Psyche And Soma

In 1900 Freud called the dream the royal road to the unconscious. From 1910 to 1955 little more was learned about the dream state of sleep. It is probably true that as much has been learned about the state of sleep in the past 15 years as in all the previous years of recorded history. This great expansion of knowledge in such a short time raises a number of interesting issues. One of these is related to the pace of scientific advances, a pace which is rarely evenly progressive.

In most fields the pace is characterized by periods of slow diligent work by a number of experts often basic scientists who communicate largely with one another. There then comes a methodological breakthrough either technical as in the case of the Rontgen ray or conceptual as in the case of the theory of Relativity. These are then followed by a great leap forward. When this happens the number of interested scientific investigators multiplies, general scientific awareness is aroused, and important links are forged with other investigative fields and disciplines. Sometimes considerable cross fertilization occurs which may lead to the birth of new subspecialties with distinctive identities.

Something of this sort has taken place in the area of sleep research. It is fitting that the breakthrough—the discovery of rapid eye movements (REM) sleep and its association with dreaming took place in the physiological laboratory of Dr. Nathaniel Kleitman for he was one of the lonely experts working in comparative obscurity. What is notable about the leap forward which followed this breakthrough is the speed with which it occurred and its wide international and interdisciplinary scope. Important contributions have come from all over the world both east and west. Much of the early research with humans was done by psychiatrists, but now neurologists, internists and psychologists have joined the field. Now all the basic neuroscientists have distinguished representatives who are active in sleep research.

The widespread interest in the field is not surprising. We are asleep for a third of our lives and spend about 20 per cent of that time in the dreaming. The neurophysiological and biochemical mechanisms underlying sleep involve neurological studies and neurochemical processes which are fundamental in mammalian arousal, emotion, consciousness, and possibly memory storage and other cognitive functions. All of this is reason enough for wanting to know as much as possible about sleep. Two factors have led to rapid productive mobilization of international and interdisciplinary resources. One is the modern scientific communication network and the other is the support of some agencies which make large-scale research possible financially. In 1965 alone the National Institute of Mental Health awarded more than 2 million dollars for over 60 projects related to the study of dreams[1] and this figure has since been surpassed.

We are therefore in a position now to move rapidly along promising avenues of research sometimes at breakneck speed, as illustrated by the flow of data and testable hypotheses which have emerged from sleep laboratories. In such a situation one must be on guard against being swept away prematurely by enthusiasm in such a field. As Lowy points out[2] many aspects are preliminary and are based on work with small samples of patients. There is a great need in a new area of investigation, both for interlaboratory verification of findings and for standardization of methods, processes, which are not yet well developed in sleep research.

It is still too early to apply clinically most of the interesting findings in this field although the recognition of the role of hallucinatory dreaming in the production of coronary attacks has greatly improved the prospect for reducing the incidence of these attacks by measures to convert hallucinatory dreaming to more thoughtful ones. From the theoretical point of view, however, there is much to be gained by vigorous interdisciplinary testing of promising hypotheses. As Platt[3] has noted with respect to molecular biology and high energy physics, rapid scientific advances depends on the use of strong inference which Chamberlain called the method of multiple working hypotheses.

Perhaps the most intriguing aspect of sleep and dream research is the possibility that it will take us one step further toward clarifying the old mind-body problem.[4] This historically has been a divisive conceptual road block in psychology, neurology and psychiatry. Today the problem is essentially one of methodology. The basic unity of mind and brain goes all but unchallenged. Students of human behavior must still choose between two fundamentally different approaches.

One is the physical chemical approach which has produced the best body of knowledge we now have about the body. But it is inadequate for the understanding of human experience. The other is psychological and depends directly or indirectly upon the introspection of the subject being studied or upon inferences made by the experimenter based upon the latter's introspection of his own experience. This approach also has led to a considerable understanding of many psychic processes to say nothing of philosophy, religion and esthetics. Unfortunately this method rarely yields quantifiable data or information which can be accurately transmitted.

Much has been done to counter these difficulties. Nevertheless there are only rare instances of fruitful unions between the two approaches. The sleep research team is the most recent illustration of such a union. It is now possible to predict that improved techniques will permit stimultaeous study of neuronal processes, peripheral physiologic responses and the stream of mental activity all to be understood in the context of the individual sleeper's personality and current psychosocial life.

It may well be then that Freud's concept of the dream as the royal road to the unconscious, will also lead to a new bridge between psyche and soma.

L.H.N.

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Prevention Of Cancer

"Even if the causes of cancer were miraculously removed . . . . Cancer would still be occurring 50 years from now owing to the long latent period between the stimulus and occurrence of the disease".—E. Boyland in a Chemist's view of the Cancer Problem.

Many types of cancer as in the case of communicable diseases may be prevented or avoided even before we are able to solve the complexities of their induction and pathogenesis. At present 85 per cent of human cancer is attributable to carcinogens. This opens up the prospect that human cancer in large part may be eradicated by the more precise identification of environmental carcinogens and their elimination. For example, we have known since 1895 of the high incidence of cancer of the bladder among workers exposed to aniline dyes. We have since learned that it was not the aniline dye per se but an aromatic amine with a methyl radical contaminant that was the carcinogen.[2] Azo dyes—butter yellow as an additive to hairdressing oils—was also demonstrated to be carcinogenic in 1962.[2]

Then there are the estrogens in some varieties of clover which cause reproductive disturbances in sheep in which even small amounts might facilitate the growth of estrogen dependent mammary tumors. Cycad seeds and induction of intestinal neoplasms in rats has been well investigated by Lacqueur.[3] Then there are other carcinogens, aflatoxin B & C derived from aspergillus mold, potent producers of hepatoma in animals.

Some naturally occurring products act indirectly. The enzyme thiaminase found in bracken fern destroys vitamin B and contains a factor which also damages white blood cells and also produces intestinal tumors in rats fed a diet containing dried bracken. Each year new chemicals are synthesized for use in industry and medicine that require careful evaluation with reference to their potential carcinogenesis. For example, griseofulvin can produce hepatic tumors when fed orally to mice. However, it cannot be overemphasized that the extrapolation to man of carcinogenic activity in experimental animals needs to be integrated with human environmental field studies before any conclusions about effects on man can be verified.[4]

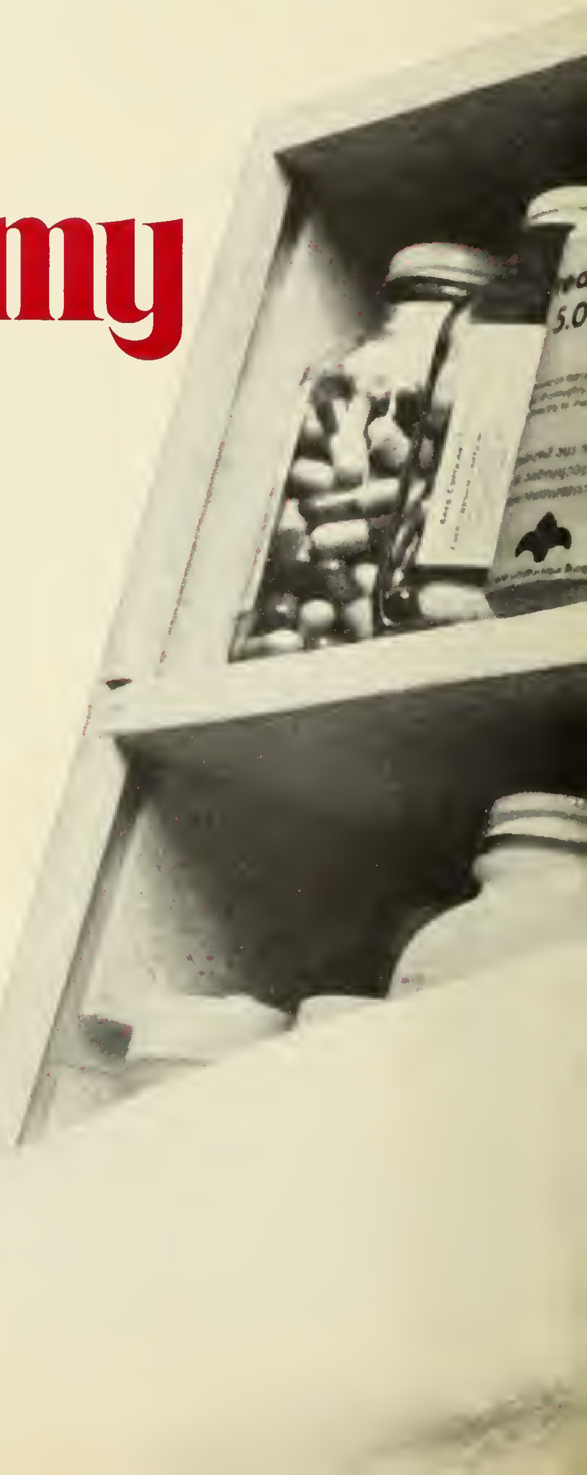
Isoniazid a potent therapeutic agent in tuberculosis and apparently harmless in doses taken, does exhibit carcinogenic potential in some animals in large doses. In the absence of adequate supporting data based on environmental biologic standards, decisions regarding utilization of therapeutic and chemical compounds will continue to be made on an arbitrary basis thus requiring society to live with situations involving calculated risks. Isoniazid might have been banned as a potential carcinogenic hazard, if present regulations had been in force earlier.

We could expand our epidemologic research to provide new knowledge. One way would be through collaborative studies in environmental biology in the form of biometry and cancer registry and differences in histologic pattern. Then there is the role of epidemiologic studies in migrant populations. Important clues have been obtained recently from studies showing a high incidence of cancer of the stomach in Iceland and Japan. A reduced incidence is present among migrants and their descendants in Hawaii and California. Then there is the increased incidence of cancer of the large intestine in Poles who emigrated to New England urban rather than rural areas.

The concept that highly carcinogenic agents occur as contaminants cannot be disregarded. Nitrosoamines are highly selective carcinogens in the induction of cancer in rat esophagus. Diethylnitrosoamine is present in Malawi gin.[4] Its presence signals a great need for relatively simple screening methods to detect such contaminants in alcoholic and other beverages and in foodstuffs. We need to know something about the distribution of certain types of tumors in domesticated or wild animals in a given region as it is related to the distribution of human tumors in the same regions. Such studies on a small scale are underway in Alameda and Contra Costa counties in California.

Trophoblastic disease in women in the Philippines, Malaysia, Singapore, and certain areas of Africa are tenfold that found in occidental populations. One explanation might be that the reticulo-endothelial system of these women has been challenged by infestations from malaria and leishmoniasis. Then there is evidence from epidemiologic case-finding that cancer of the uterine cervix may be related to possible precursors such as trichomoniasis and herpes simplex infections, dysplasia of squamous mucosa in early stages such as are curable or reversible. Papanicolau cytologic techniques may thus be extended and become valuable also as a preventive measure.

Additional concepts regarding etiology and implication for possible cancer prevention is that of a co-carcinogen, that is a chemical or physical agent often weak by itself, which may produce neoplasms when acting together. Some carcinogens may initiate a dormant neoplastic process until other carcinogens promote or accelerate its growth. Intrinsic factors of oncogenic origin when reacting with extrinsic factors, hormones,



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genetic coding and some viruses may be co-carcinogenic.

We already know etiologic viral agents in neoplastic processes especially in the lymphoreticular systems such as leukemia[5] and Burkitt's lymphoma. We know of neoplasm induction in experimental animals by non-oncogenic human viruses. Finally we know that certain tumors induced by carcinogens will grow only in the presence of sufficient hormones.

Cancer research on an international scale has identified many environmental hazards. The elucidation of tobacco smoke as a major health hazard ranks in importance with the victories over water and food-borne killers of the preceding century. L.H.N.

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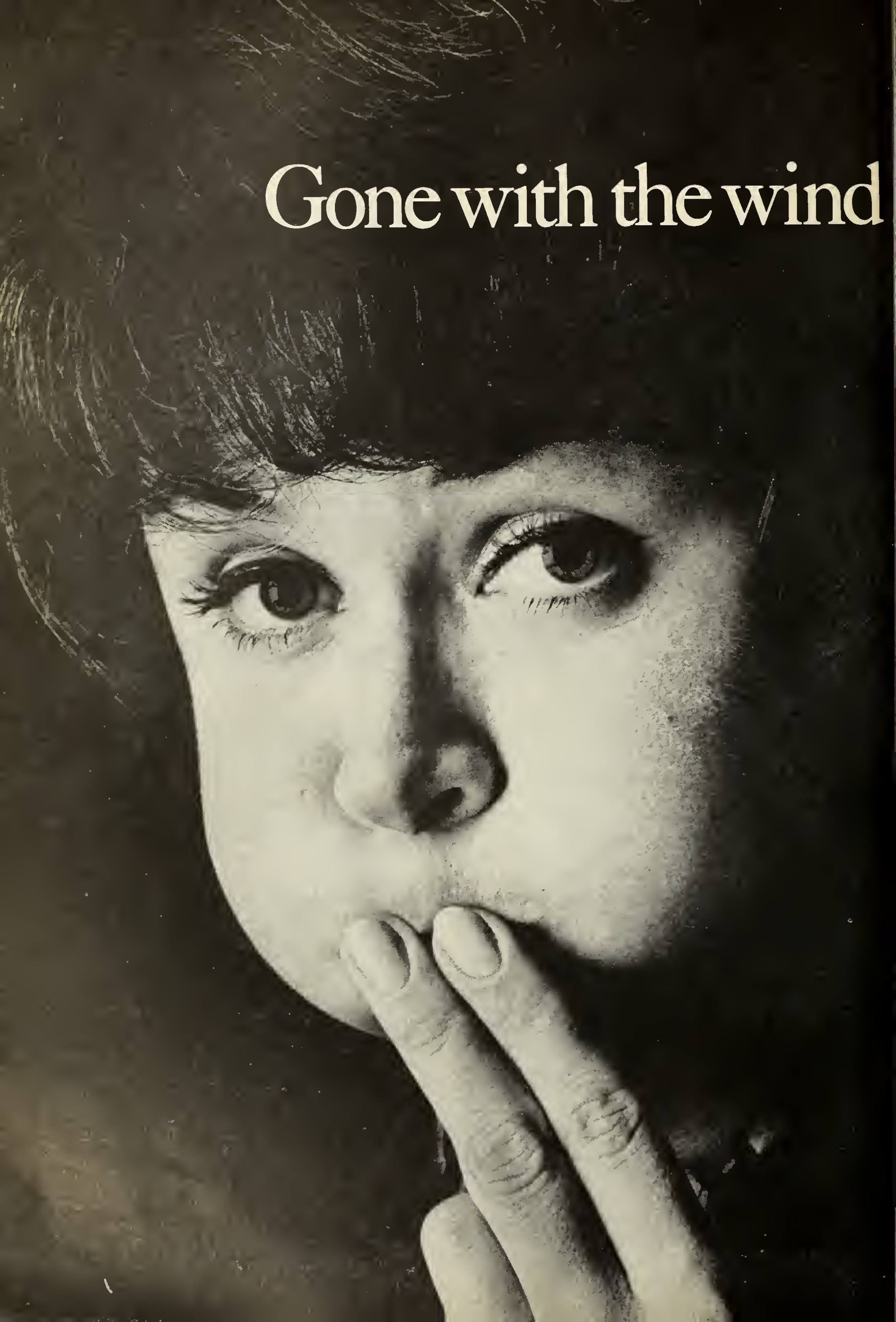
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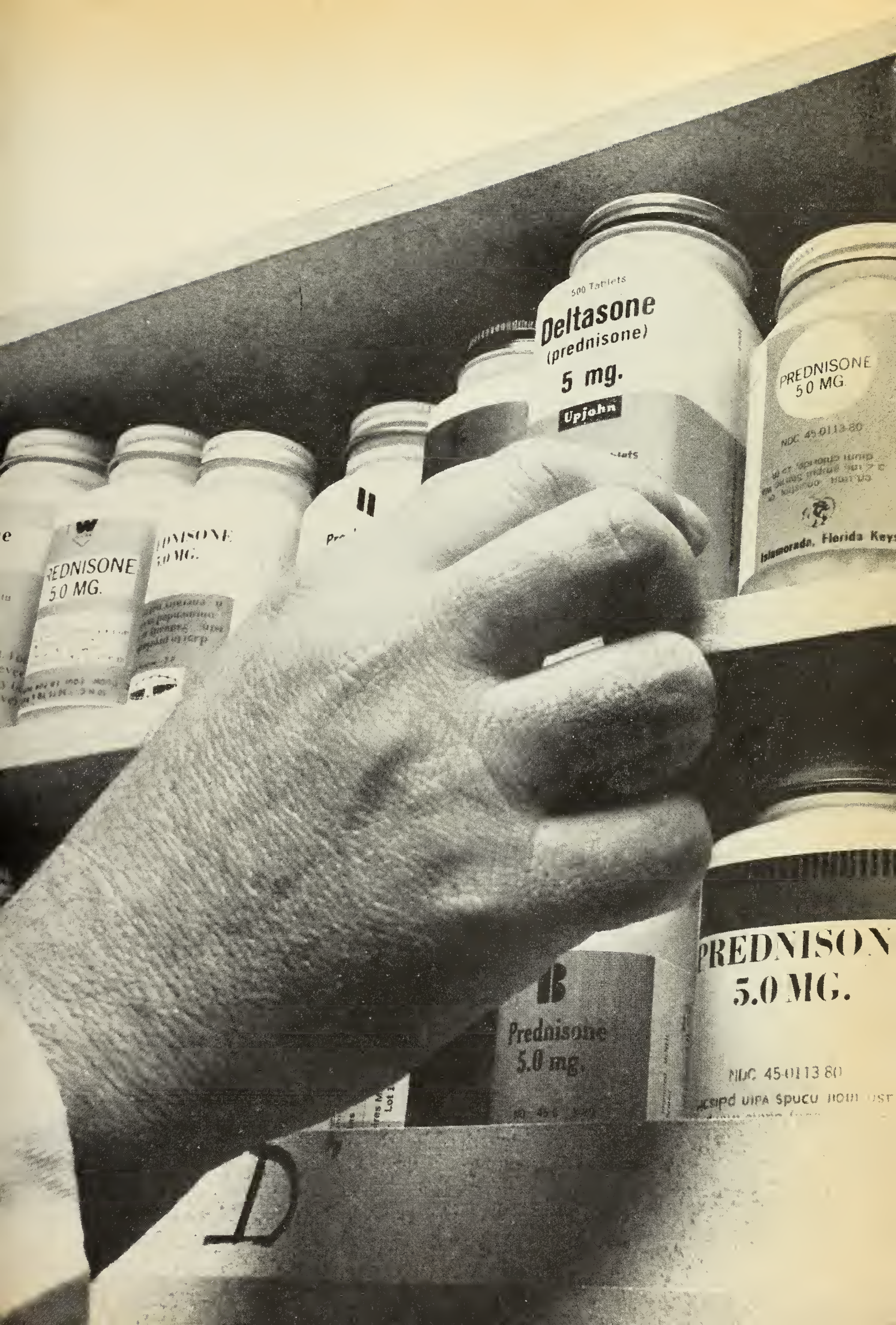
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Indications are the same as those for other anti-inflammatory steroids. Representative uses include collagen diseases, allergic diseases, generalized dermatoses, acute ocular inflammatory disease, certain lymphatic neoplastic diseases, ulcerative colitis and nephrosis. *Important:* Prednisone, like cortisone, is a potent therapeutic agent influencing the biochemical behavior of most, if not all, tissues of the body. Because it manifests little sodium-retaining activity, the usual early sign of cortisone overdosage (i.e., increase in body weight due to fluid retention) is not a reliable index. Hence, recommended dose levels should not be exceeded, and all patients should be under close medical supervision. All precautions pertinent to the use of cortisone apply to Deltasone (prednisone).

Contraindications: As for all other corticoids. *Considered Absolute*—herpes simplex keratitis, acute psychoses and latent, healed or active tuberculosis. May be lifesaving in certain cases of pulmonary or meningeal tuberculosis, but should be used only in conjunction with adequate and effective antituberculous therapy to which causative organisms are shown to be sensitive. *Considered Relative*—active or latent peptic ulcer, Cushing's syndrome, diverticulitis, fresh intestinal anastomoses, osteoporosis, renal insufficiency, thromboembolic tendencies, psychotic tendencies, diabetes mellitus, hypertension, local or systemic infections including vaccinia, varicella and other exanthematous diseases, and fungal infections, and, pregnancy particularly during the first trimester because of observation of fetal anomalies in experimental animals. If necessary to give corticosteroids during pregnancy, watch newborn infants closely for signs of hypoadrenalism and institute appropriate therapy if signs appear.

If corticoids are used in the above conditions, weigh risks against benefits.

Precautions: Deltasone should be given only with full knowledge of characteristic activity of and varied responses to corticoids. Because of inhibiting effect on fibroplasia, corticoids may mask signs of and enhance spread of infection; hence, watch patients closely, and if intercurrent infection occurs, control with appropriate antibacterial measures. If possible, avoid abrupt cessation of corticosteroid therapy because of the danger of superimposing adrenocorticoid insufficiency on the infectious process. Prolonged hormone therapy usually causes a reduction in the activity and size of the adrenal cortex. When discontinuing therapy, relative adrenocortical insufficiency may be avoided by gradual reduction of dose. However, a potentially critical degree of insufficiency may persist asymptomatically for some time even after gradual discontinuation of adrenocortical steroids. Therefore, if a patient is subjected to significant stress, such as surgery, trauma, or severe illness while being treated, or within one year (occasionally up to two years) after treatment has been terminated, hormone therapy should be augmented or reinstituted and continued for the duration of the stress and immediately following it. Since mineralocorticoid secretion may be impaired, salt and/or descxycorticosterone should be administered conjunctively. It is preferable to use a soluble hormone preparation in the immediate preoperative and postoperative periods.

Although unlikely with Deltasone, average and large doses of corticosteroids can cause elevation of blood pressure, salt and water retention and increased potassium and calcium excretion. Dietary salt restriction and potassium supplementation may be necessary. Glucocorticoid steroids may aggravate diabetes mellitus so that higher insulin dosage may become necessary or manifestations of latent diabetes mellitus may be precipitated. Corticosteroids may aggravate myasthenic symptoms in myasthenia gravis and should be given with proper precautions.

Muscle weakness, in some instances, attributed to hypopotassemia, has been reported following prolonged systemically administered corticoids. Excessive potassium loss, like excessive sodium retention, is not likely to be induced with effective maintenance doses of Deltasone (prednisone), however, keep this effect in mind and perform periodic serum potassium determinations in patients on prolonged corticoid therapy. Muscle weakness occurring with normal serum potassium levels may be due to disturbance in muscle metabolism. Severe myopathy is associated with substantial doses of steroids for prolonged periods, and evidence indicates it occurs more frequently with 9-alpha-fluro steroids. Replacement with non-fluorinated steroid has, in some instances, resulted in improvement.

Retardation of linear growth, roughly proportional to dose, has been noted in children on corticoids for six months or more. Following cessation of therapy, growth rate may be accelerated. Therefore, carefully observe growth of children on prolonged corticoid and if growth is retarded, reduce dose sufficiently to permit recovery before epiphyseal closure. Make every effort to avoid corticoids during pregnancy, since spontaneous remission of some diseases such as rheumatoid arthritis may occur. Long term corticoid therapy may evoke hyperacidity or peptic ulcer, therefore, as prophylaxis, an ulcer regimen and antacid are highly recommended. Take X-rays in peptic ulcer patients complaining of gastric distress, and, whether or not changes are noted, an ulcer regimen is recommended. Since prednisone causes less salt and water retention than many other glucocorticoids, patients should be observed closely for development of undesirable hormonal effects that are less obvious indications of steroid toxicity than edema and hypertension due to salt and water retention. Continued supervision of patients after cessation of therapy is essential, since there may be a sudden reappearance of severe disease manifestation.

Adverse Reactions: Adverse reactions associated with use of corticoids include: Cushing's syndrome, moon facies, supraclavicular fat pads, hirsutism, striae and acne; relative adrenocortical insufficiency particularly in time of stress due to trauma, surgery or severe illness; protein catabolism with negative nitrogen balance; electrolyte imbalance; alteration of glucose metabolism with aggravation of diabetes mellitus including hyperglycemia and glycosuria; osteoporosis reversible only with difficulty; spontaneous fractures; aseptic necrosis of the hip and humerus; activation and complication of peptic ulcer including perforation and hemorrhage; aggravation or masking of infection; increased blood pressure; convulsions; petechiae and purpura; menstrual irregularities including amenorrhea, spotting or prolonged bleeding; insomnia; psychic disturbances especially abnormal euphoria; nervousness; posterior subcapsular cataracts occasionally requiring extraction; increased intraocular tension; increased intracranial pressure with papilledema (pseudotumor cerebri); pancreatitis; necrotizing angiitis; thinning of scalp hair; suppression of growth in children; thromboembolic complications; facial erythema; allergic skin reactions; ulcerative esophagitis; sweating; vertigo; weakness; myopathy; headache; exophthalmos. Adverse reactions are usually reversible and usually disappear when drug is discontinued.

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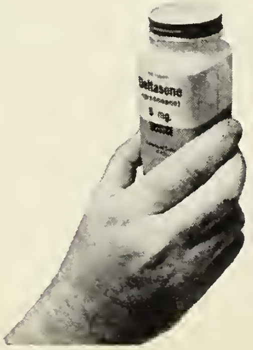

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Herpes virus continues to amaze its students. It has been recognized for several centuries, affects close to 100 per cent of individuals in certain population groups and has been identified in the laboratory for over 50 years, yet it continues to demonstrate heretofore unrecorded manifestations in certain patients. Some of the complexities of herpes-simplex virus can well be appreciated now that it has been found that there are two antigenic types with different biologic and epidemiologic characteristics. Students are mystified by its ability to recur (latency, chronic infection, reinfection). They are puzzled by the actual extent of its pathogenicity in human beings for example, the recent observations linking genital herpetic infections with cervical cancer, as well as fetal and newborn disease.

The manifestations of herpetic infections have ranged from subclinical infections to severe fatal disease with involvement of any part of the body, skin, eyes, genitalia, lips, can become involved with frequent recurrences at the same site and aside from corneal infections that may lead to blindness medical concern has focused principally upon the virus involving the brain or visceral organs since infection at these sites results in neurological sequelae or even death. We do not know the type of host most susceptible to herpetic encephalitis. From clinical experience we know that newborn particularly, the premature infants, grossly malnourished persons such as those with kwashiorkor; patients with associated infections particularly measles,[2] those undergoing immuno-suppressive therapy or having cellular immune defects such as Hodgkins or Wiscott-Aldrich syndrome, patients with underlying skin disorders particularly atopic eczema and now burns.

The physician must be alert to the possibility of viral dissemination or extensive local herpetic infections in such cases. They are not the result of absence of antibodies, since the infection may occur when antibodies are present in the blood. There are certain common denominators among the susceptible person: underlying skin disorders, low serum protein levels and inadequate cellular immune responsiveness[3].

Available diagnostic methods are multiple: demonstration of herpetic mechanisms or cytologic or histologic specimens, recovery of virus by tissue cellular methods from skin or body orifices, from blood, urine, special fluid or biopsy material and demonstration of the virus in smears of lesion or in biopsy or autopsy material, by electron microscopy or fluorescent antibody techniques. The recent finding by Nahmias[3] that IGM antibodies to herpes-simplex virus can be detected in serum obtained soon after the onset of infection might also prove helpful in early diagnosis.

Once the diagnosis is confirmed we are left with a therapeutic dilemma. At present large doses of commercial gamma globulin which contains relatively high titers of herpes simplex neutralizing antibodies is available but in practice it does not prevent blood dissemination of the virus. Another possible but less accessible approach recently recommended for the treatment of herpetic encephalitis is systemic use of idoxuridine[4]. However, we need well-controlled studies to determine the effectiveness of the drug in such severe herpetic disease. Other more theoretical approaches to treatment that need concerted study are the use of interferon inducers such as poly-O-poly-C and transfusion with sensitized lymphocytes or their active factors.

Complete prevention of herpetic infection such as might be accomplished with vaccines also awaits better biochemical and immunopathologic definition of the illusive herpes virus and its multifarious clinical expressions. In the meantime it would be of interest if pathologists reviewed organ sections from autopsied patients with burns in search of herpetic infections, now that Foley et al have shown that herpetic infection may not be an infrequent cause of death after burns.

L.H.N.

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Report Of The Council On Environmental Quality, Facts And Recommendations

The meat of the report is a description of the damage done and the problems to be faced. Only one-third of the population of the U.S. is served by an adequate sewage system and another third has no system. By 1980 one fifth of the total fresh water runoff will be required for cooling operations of the electric power industry. The refuse collected for each town dweller in the U.S. has grown from 2.75 pounds a day in 1920 to 5 pounds in 1970 and will reach 8 pounds in ten years time. In 1969 Americans threw away about 250 million tons of solid wastes of which three quarters was collected and the rest junked. The collected wastes include 30 million tons of paper, 4 million tons of plastic, 100 million tires, 30,000 million bottles and 60,000 million cans.

Among the uncollected trash is some 15 per cent of the 9 million cans abandoned each year and between 1-2 billion bottles and cans. There are prospects of recycling some of this litter if it could be collected. The only direct use the council has come up with is for automobile tires which it is suggested could be used to make artificial reefs for fish breeding along the flat ocean bottom off the Atlantic coast.

The Council's report was prepared by Russel E. Train formerly undersecretary of the interior and president of the Conservation Foundation from 1965 to 1969. His two colleagues are Robert Cahn on leave from the Christian Science Monitor and a specialist on national parks and Dr. G. J. F. MacDonald, a physicist who has served on the President's Scientific Advisory Committee. The report is a compendium of facts and recomendations about the environment. It represents the first attempt in the U.S. and probably in any other country to consider the whole range of points at which the environment has been altered by man to their mutual detriment. The report describes the various types of pollution that befoul the air and waters and suggests how each should be combatted. Many of the 50 or so specific recommendations made in the report have already been embodied in legislative proposals sent to congress early this year which are still awaiting decisions.

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The Council has not been content to deal only with smog, sludge and oil slicks but has lifted its sights to include the pressures of population on land and on scarce natural resources. From there it goes on to consider the more fundamental question of whether economic growth should be restrained for the sake of conserving the environment. This perhaps is the crucial point at which ecological perfectionists part company from the rest. The Council in its own words has taken a broad view of the term environment and this broader view reveals many benefits of continued economic growth. They believe our society needs more goods and services of many kinds, better housing, improved public transportation, more adequate facilities for health and education and increased pollution control.

It is likely that funds for such investments will come not from a cutback in the production of cosmetics for example but from an overall incerase in GNP. Moreover a reduction in growth would result in a severe blow to the aspirations of the economically disadvantaged especially the minority groups. This is not to say that the economy can remain unaffected by the attempt to preserve the environment. The Council does not remark on the wasteful practice of introducing rapid obsolescence in automobiles and other goods which require frequent replacement. It does remark that in the long run the control of water pollution may require some changes in the products that people use up and will lead to higher prices in some products.

A major theme of the report is that pollution is at present being encouraged by misplaced economic incentives and that the cost of preventing pollution is borne by the community downstream or downward of the factory instead of by the manufacturers and his customers. These "external social costs" should be reflected in the price system instead of by society as a whole. Another type of misplaced incentive is the property taxes which lead to bad land use by encouraging local governments to favor industrial developments against houses which cost more in terms of the schools and hospitals which accompany them than they yield in property taxes.

What the Council's recommendations boil down to is first and foremost that congress should not drag its feet with the substantial volume of legislative proposals on the environment that are already before it. These include the setting up of an Environmental Protection Agency to gather together under its wings the bits and pieces of environmental control developed by other agencies and the National Oceanic and Atmospheric Administration which do the same for oceanography and meteorology.

Besides the strengthening of the institutional structure for protecting the environment the Council also makes numerous proposals by which changes in the environment such as mercury pollution of lakes for example will be spotted not too late in the day. Doubtless if all the recommendations were honestly carried out we would have a better world to live in. But what the Council does not deal with is the all too common occurrence where the polluters are also administrators of the laws. L.H.N.

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Gram Negative Septicemia

Gram negative septicemia was recently a subject of discussion at the Royal Society of London[1]. The recent figures from London show that the incidence of bacteremia, both gram negative and gram positive, is around 2.1 per 1,000 admissions, a figure which is lower than in this country[2]. In the teaching hospitals most of the bacteremias developed after admission. In the suburban hospitals the patients were already bacteremic on admission.

Both gram negative and gram positive patients present the same clinical picture. This may be confusing since patients often have suffered from other serious illnesses and therefore react in unorthodox ways to a flood of bacteria in the blood. In the early stages of septicemia there may be pyrexia with chills. This can give rise to two pictures of shock. The first is a "warm hypotension" picture with a warm dry skin but low blood pressure. The other is the classical picture of peripheral circulatory failure with cold moist skin, pallor, sweating, anxiety, dyspnea and cyanosis. The presence of shock which is more commonly seen nowadays means an increase in mortality and is reported to develop in 15-20 per cent of cases of gram negative sepsis.

The commonest gram negative organism is E. coli, Proteus, Klebsiella, pseudomonas and salmonella are far behind. The urethra seems to be the commonest point of entry. Some are preceded by a urinary tract infection and others by infection of the gastrointestinal tract. The septicemia is often secondary to some debilitating illness such as cancer, chronic urinary tract infection, recent abdominal surgery. Especially hazardous is the gram negative infection following renal transplant. Insertion of an intravenous or urinary catheter is a common forerunner and antibiotic or steriod therapy may have been given. Bacteremic shock must be differentiated from such conditions as hemorrhage, pulmonary embolism, coronary heart disease or respiratory insufficiency. Blood cultures are essential and laboratory services must be used freely to establish antibiotic sensitivity as well.

Treatment requires early diagnosis and appropriate therapy. The mortality rate fell from 53 to 24 percent. The most suitable antibiotic, Kanamycin, seems to be the first choice.[3] This antibiotic, however, is of no value in pseudomonas. Chalmers and Tiller[4] gave 1 gram intravenously immediately then 250 mg every 8 hours. Some specialists consider genta-micin the first choice when septic shock is present and give 80 mg every 8 hours. If pseudomonas is the offending organism, they advised a loading dose of carbenicillin 160 mg. Obviously pus when present should be drained.

If shock is present then fluid replacement is needed. The best guide is the central venous pressure which should be kept at 10-15 ml water. After this, experts differ but generally agree that vasopressor agents should not be used. There

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WARNINGS: Patients should be warned against driving a car or operating machinery or apparatus requiring alert attention, and that response to alcohol may be increased.

PRECAUTIONS: Suicide is always a possibility in mental depression and may remain until significant remission occurs. Supervise patients closely in case they may require hospitalization or concomitant electroshock therapy. Untoward reactions have been reported after the combined use of antidepressant agents having various modes of activity. Accordingly, consider possibility of potentiation in combined use of antidepressants. Use with caution in patients with glaucoma and those with problems of urinary retention. Perphenazine can lower the convulsive threshold in susceptible individuals. It should be given with caution to patients with convulsive disorders. Dosage of the anticonvulsive agent may have to be increased. Not recommended for use in children. Mania or hypomania may be precipitated in manic-depressives (perphenazine in TRIAVIL seems to reduce likelihood of this effect). If hypotension develops, epinephrine should not be employed, as its action is blocked and partially reversed by perphenazine. Caution patients about errors of judgment due to change in mood.

ADVERSE REACTIONS: Similar to those reported with either constituent alone.

Perphenazine: Should not be used indiscriminately. Use caution in patients who have previously exhibited severe reactions to other phenothiazines. Likelihood of untoward actions greater with high doses. Closely supervise with any dosage. Side effects may be any of those reported with phenothiazine drugs: extrapyramidal symptoms (opisthotonos, oculogyric crisis, hyperreflexia, dystonia, akathisia, dyskinesia, parkinsonism) usually controlled by the concomitant use of effective antiparkinsonian drugs and/or by reduction in dosage, but sometimes persist after discontinuation of the phenothiazine; skin disorders (photosensitivity, itching, erythema, urticaria, eczema, up to exfoliative dermatitis); other allergic reactions (asthma, laryngeal edema, angioneurotic edema, anaphylactoid reactions); peripheral edema; reversed epinephrine effect; hyperglycemia; endocrine disturbances (lactation, galactorrhea, disturbances of menstrual cycle); altered cerebrospinal fluid proteins; paradoxical excitement; EKG abnormalities (quinidine-like effect); reactivation of psychotic processes; catatonic-like states; autonomic reactions, such as dryness of the mouth, headache, nausea, vomiting, constipation, obstipation, urinary frequency, blurred vision, nasal congestion, and a change in the pulse rate; hypnotic effects; pigmentary retinopathy; corneal and lenticular pigmentation; occasional lassitude; muscle weakness; mild insomnia. Other adverse reactions reported with various phenothiazine compounds, but not with perphenazine, include blood dyscrasias (pancytopenia, thrombocytopenic purpura, leukopenia, agranulocytosis, eosinophilia); liver damage (jaundice, biliary stasis); grand mal convulsions; cerebral edema; polyphagia; photophobia; skin pigmentation; and failure of ejaculation. Significant unexplained rise in body temperature may suggest intolerance to perphenazine, in which case discontinue. Antiemetic effect may obscure signs of toxicity due to overdosage of other drugs or make diagnosis of other disorders such as brain tumors or intestinal obstruction difficult. May potentiate the action of central nervous system depressants (opiates, analgesics, antihistamines, barbiturates, alcohol) and atropine. In concurrent therapy with any of these, TRIAVIL should be given in reduced dosage. May also potentiate the action of heat and phosphorous insecticides.

Amitriptyline: Careful observation of all patients recommended. Side effects include drowsiness (may occur within the first few days of therapy); dizziness; nausea; excitement; hypertension; fainting; fine tremor; jitteriness; weakness; headache; heartburn; anorexia; increased perspiration; incoordination; impotence; increased appetite and weight gain; allergic-type reactions manifested by skin rash, swelling of face and tongue, itching; numbness and tingling of limbs, including peripheral neuropathy; activation of latent schizophrenia (however, the perphenazine content may prevent this reaction in some cases); epileptiform seizures; temporary confusion, disturbed concentration, or transient visual hallucinations on high doses; evidence of anticholinergic activity, such as tachycardia, dryness of mouth, stomatitis, blurring of vision, reversible dilatation of the urinary tract, urinary retention, constipation, paralytic ileus; agranulocytosis; jaundice. Elderly patients and adolescents can often be managed on lower dosage levels.

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are some who use adrenergic blocking agents such as phenoxybenzamine and betareceptor stimlulants like isoproterenol. Opinion was divided among the experts on the benefits of steroids in bacteremic shock. There are a few American consultants who support their use, but Chalmers and Tiller found the evidence in their series quite equivocal.

A new menace has appeared on both sides of the Atlantic. It was formerly thought that the gram negative organism formely known as P prodigiosus and now termed Serratia marcescens was a harmless saprophyte. However, in 1969 both American and French authors have reported series of cases of sepsis caused by this organism. Altemeir et al[5] collected 42 cases in Cincinnati in seven years mostly related to antecedent or concurrent antibiotic therapy.

The source of the infection was usually the urinary tract, a thrombo-phlebitic lesion at the site of an intravenous drip or the respiratory tract after assisted ventilation or tracheostomy. The picture was the same as that of other gram negative septicemia and the mortality rate 40 per cent. Most strains of the organism were sensitive to Kanamycin or chloramphenicol.

In Paris, Vic-Dupont et al collected 26 cases at a resuscitation center. In every case there had been a combination of antibiotic therapy plus a serious illness plus the use of some technique permitting infection such as bladder catheterization intra-venous infusion, tracheostomy or dialysis. These workers found gentamicin and nalidixic acid almost always effective. L.H.N.

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Prediction From College Grades

Do college grades predict anything about a person's future achievement? Kirk in a letter to *Science* on Jan. 9, 1970 states that college grades in fact are poor predictors of anything in post-collegiate biographies. To be sure, correlations are not as high as those between entrance tests and grades, but indications of a positive relationship between college grades and what happens afterward in "real life" are clear. Somehow or other the idea that college grades are unrelated to what happens to the individual later seems to be a permanent feature in the mythologies of academia in spite of overwhelming evidence to the contrary.

Havemann and West in 1952 surveyed college graduates of all ages and noted that those who have been A students tended to earn more than those who earned B's, and these in turn earned more than those who earned C's and D's. The difference between A students and others was particularly marked, especially in science, medicine, and law. A more recent study was conducted by Oden[3]. He classified members of Terman's gifted group who were then in their 50's according to a number of success-oriented characteristics. He then selected a "most successful" and "lease successful" group for further investigation.

Oden found many interesting and significant differences between the two groups. The one that is important to the question of grades as predictors is that the most successful group had a much higher percentage of A students, and had been awarded more academic honors than the least successful. Of course, we must remember that college professors, like a great many people, evaluate and pass judgment on an individual's performance during his lifetime. It is hardly surprising that the kind of success which people display in coping with the problems we encounter during college tends to be characteristic of the success we have in other areas. To be sure, there are many individual instances of uneven and inconsistent performance, which tend to attract notice because they are unusual. On the whole, however, if the study of personality has shown anything at all, it is that people are more consistent than otherwise.

The general trend is toward a general consistency in individual performance. This is, of course, in turn reflected by consistencies in the way different judges, official and otherwise, evaluate the same individual's performance. This tends to be true regardless of whether the judges are teachers, employers, workers, casual acquaintances, one's family, or even one's students. The basic consistency in behavior of both the evaluated and the evaluators shows up in positive correlations among measures of such variables as grades, leadership, social adjustment, and even general problem-solving.

The important point is that although behavior tends to be consistent, this does not mean that behavior cannot be changed, but rather that changes do not occur very readily. It is the major function of education to bring about desirable changes. When we fail in this, it may in large part be due to our inability to attain a more meaningful understanding of the phenomena which we are trying to modify.

L.H.N.

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Tracking The Y Chromosome

Dr. T. Casperson and his colleagues showed two years ago that certain fluorescent derivates of acridine stain the chromosones of various organisms. Last year Dr. Laura Zech and her colleagues noted that quinacrine mustard makes part of the human Y chromosome fluoresce particularly brightly. This illuminating finding has been taken up in several laboratories and important discoveries seem to be emerging faster than they appear in print.

Two months ago Pearson, Bobrow and Vosa demonstrated that the quinacrine straining test shows up the members of Y chromosomes in a human non-dividing cell (interphase). This is an important timesaver for those engaged in screening human populations for XYY males, the possessors of an extra Y chromosome who as adults tend to be found in persons slightly more often than it seems they should be. Hitherto, the only way to identify the extra Y chromosome has been the laborous task of culturing leucocytes and doing a full karyotypic analysis. The quinacrine test is the exact counterpart of the simple stain for the Barr body which shows up in the presence of extra X chromosomes which led indirectly to the discovery of XYY males in the first place.

There has been an academic issue of 30 years standing as to whether it is the short arm or the stem of the Y chromosome that is associated with the X chromosome in meiosis. Pearson and Bobrow have now used the quinacrine technique to show that it is the short arm. Furthermore, Bobrow and Voza have now been able to differentiate the male determining spermatozoa from the female determining one by using the stain on human spermatozoa. No wonder that a fever of excitement among cytogeneticists is being whipped up by quinacrine hydrochloride. The technique will certainly afford a useful test of success for those who are trying to separate male and female determining sperm as a means of sex control.

Admittedly we are not yet at the control of sex if only because this dye almost certainly kills as it distinguishes. In any case the quinacrine stain or others like it should provide a simple test for assessing the various methods whether based on centrifugation or electrophoresis whereby people have sought to separate the two kinds of sperm. In the past the outcome of such methods have been uncertain because it could only be tested by animal breeding.

The animal breeders' enthusiasm may be a bit premature, however. Quinacrine appears not to distinguish the Y chromosome of Bull spermatoza since it stains all chromosomes equally. It may be that man is unique among mammals in this respect. However, even if quinacrine is selective only in man, its use in this species is not restricted to the Y chromosome. Pearson at Oxford found that certain of the autosomes took up the stain in a way that depends on the individual.

The acridine dyes certainly hold a lot of interesting secrets in store. The immediate results probably will be in solving straightforward cytogenetic problems as well as in clinical medicine and genetic counselling. The new technique will certainly hasten the rate of progress in human cytogenetics and the next five years should see a number of fresh insights opened into the behavior of chromosomes in cells.

L.H.N.

Reference

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Fetal Goiter Due To Iodide Ingestion By The Mothers

Maternal ingestion of iodide has been implicated in the causation of congenital goiter since 1940 when Parmlee et al reported 3 cases of newborn infants with goiter. All three mothers had taken iodide containing preparations thoughout pregnancy. None of the mothers had goiter. Since then sporadic cases of similar goiter have been reported. The infant's goiter usually regresses within months of birth. Iodide goiters have also been reported to occur in adults. Despite these reports congenital iodide goiters often with hypothyroidism are still occurring and iodide containing preparations are still freely available to the public.

The list of drugs which have been reported to harm the unborn child if taken by the mother continues to increase, so that most doctors now avoid giving any drugs in pregnancy unless there are strong indications. Sometimes, however, the risk to the mother of withholding treatment justifies exposure of the fetus as for example in the chemotherapy of malignant disease. Similarly the small risk of 8th nerve damage to the fetus can be accepted if the mother must have streptomycin for tuberculosis.

Often, however, possibly harmful drugs have been given for much less pressing reasons. Furthermore, the risk to the fetus of proprietary medicines which can be bought over the counter have not been fully assessed. In their article Carswell reports 8 cases of congenital goiter and hypothyroidism caused by iodide containing medicines taken by the mothers. These medicines were taken as expectorants and cough suppressants for asthma and bronchitis and several of them did not require a doctor's prescription. Two of the women were taking more than 1 gram of iodide daily from such preparations.

As a result of iodide ingestion by the mother, the thyroid of the fetus may become very large and pressure on the trachea may interfere with respiration. Although some infants have been euthyroid, many others show evidence of hypothyroidism with retarded bone development, mental impairment and even cretinism. Even prompt treatment by controlled respiration, thyroid replacement and antibiotics failed to save the lives of some of the children.

It is important, therefore, that iodide containing preparations should carry warnings of their potential dangers during pregnancy. Even more desirable they should be available only by a doctor's prescription. Iodide toxicity is not the only hazard of medicines taken for the relief of asthma. Many preparations contain sympathomimetic amines such as ephedrine which have their own dangers, particularly interaction with monoamine oxidase inhibitors in patients being treated for depression or hypertension. The dispensing of ephedrine containing tablets is closely controlled. However, liquid preparations are sometimes available without prescription.

More should be done to make the public aware that certain drugs even though they may be available without a prescription, are pharmacologically highly active and that pregnant women should never take them unless they have been prescribed by a physician. L.H.N.

The Government Downgrades Cancer Research

> *If I had my choice between a moon walk and the life of a single child with Leukemia, I would never glance upward—*
>
> James T. Grace, Jr., M.D.

The last decade saw the development of concepts of curability of cancer hitherto thought incurable. One example is that of Hodgkins Disease when obtained early can be successfully treated with radiation and drugs. The concept of curability of acute leukemia was thus born. All children died a few weeks or months after diagnosis and with much suffering. Now three-quarters are living after two years. Another bright spot is Burkitt's lymphoma formerly uniformly fatal and now amenable to successful cure with drugs. Other forms of childhood cancer, formerly highly lethal like Wilms' Tumor, are now being successfully treated with surgery, radiation and drugs.

There is also a veritable mountain of exciting laboratory research whose potential in the control of human cancer has not yet been explored. The search for viruses that cause human cancer has been greatly intensified. There is considerable evidence that they may play a role in human malignant disease and further knowledge could have considerable practical importance both in cancer prevention as well as in treatment.

Another exciting field of cancer research involves stimulation of the body's normal defenses against cancer. This has already been done quite successfully with animal cancers and with be-

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Contraindications: Hypersensitivity to barbiturates or belladonna alkaloids, glaucoma, advanced renal or hepatic disease.

Precautions: Administer with caution to patients with incipient glaucoma, bladder neck obstruction or urinary bladder atony. Prolonged use of barbiturates may be habit-forming.

Side effects: Blurred vision, dry mouth, dysuria, and other atropine-like side effects may occur at high doses, but are only rarely noted at recommended dosages.

Dosage: Adults: One or two tablets three or four times daily. Dosage can be adjusted depending on diagnosis and severity of symptoms. Children 2 to 12 years: One half or one tablet three or four times daily. Tablets may be chewed or swallowed with liquids.

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to move,
and the Latin **sedatus**,
to calm)

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ginning success in a limited number of human cases. Many investigators believe that a combination of this approach with other established forms of treatment could substantially advance cancer control. All these leads need rapid expansion to make them available to the cancer patient as soon as possible. This calls for large new research programs that cost money.

More than one-half of the 1970 fiscal year has passed and the National Cancer Institute has been operating on an annual budget of 173 million which is 12 million less than fiscal '69. After much maneuvering in which the President threatened to veto an appropriation of 190 million, he signed an appropriation bill at about 181 million. Regardless of what happens, the damage for this year has already occurred. This means that biomedical research has been downgraded in national priorities. This, in spite of the fact that there is literally nothing that will more surely improve the quality of American life than health research. This is our only hope of really controlling devastating diseases and their enormous cost. A cure for cancer would do more for our citizens than a thousand regional medical programs at a fraction of the cost.

Cancer will strike one out of four living Americans. It is the number one killer of children and costs Americans 15 billion annually not counting the suffering and grief which cannot be measured. The National budget for 1970 is 193 billion roughly $964 for every American. The Vietnam war's share is $125. Each American's share of cancer research is 91 cents or 1/150th of the Vietnam war cost.

One billion dollars was poured into an atomic powered airplane program and 10 million into a structure to hold an airplane that was never built. This is seven times the National Cancer Institute's (NCI) budget. President Nixon wants 553 million instead of 336 for the Alliance for Progress in Latin America.

The increase is 1¼ times the NCI budget. President Nixon also wants to increase the 1.3 billion for foreign economic aid to 2.3 billion. Just the increase is 6 times greater than the total NCI budget. Last year a minimum of $350 million was spent on research, on chemical and biological warfare. This is double the amount spent for cancer research.

How can this be explained to the young parent of the child with leukemia or the husband of a young mother with disseminated breast cancer? It is clear that there are serious questions about our government's view of national priorities. It is up to an informed citizenry to speak up loudly enough and often enough, for only then will it be heard.

An informed citizenry should understand that the awful history of cancer could be written in the next decade. The prospects, however, are sharply hindered by present priorities of federal spending in which there is more interest in research in chemical and biological warfare than in cancer research.

To weather the crisis increased support of cancer research is imperative. The seventies can be a decade of hope for the 50 million of us destined to develop cancer in the future. We were all awed by the magnificent space achievement of the sixties but, "If I had a choice between a moon walk and the life of a single child with leukemia, I would never glance upward", so spoke Dr. James T. Grace, Jr. L.H.N.

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Vitamin E. Deficiency

When vitamins were first discovered a wave of enthusiasm about their value spread to engulf every patient and every doctor in every disease. The pendulum has now swung to the opposite extreme where it is stated that all people eating "properly" cannot be vitamin deficient. In consequence we are probably missing many opportunities to assist some of our patients to a more healthful nutritional state. For example we have learned from the role of vitamin B_{12} in nutrition that there can be dangerous depletion states particularly of the brain and peripheral nervous system long before anemia becomes the signal for the search of this syndrome.[1]

Now we find a similar story about vitamin E (tocopherol). Vitamin E deficiency was discovered forty-six years ago. Because human adults made vitamin E deficient have not had clinical manifestations it was assumed, deficiency of this vitamin is not a significant occurrence. Nevertheless animal studies have shown notable damage when rendered vitamin E deficient and human adults deficient in this vitamin will have more ready hemolysis of their red cells when

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Menrium takes care of hot flashes, vertigo, palpitations in most menopausal women. Menrium provides the well-known antianxiety action of chlordiazepoxide (Librium®) and water-soluble esterified estrogens. It therefore relieves more symptoms than either component separately. It takes care of the vasomotor symptoms as well as the emotional symptoms. This means the symptoms that bother his wife most. And the symptoms that irritate him most.

So, to help them both get through *her* menopause, remember Menrium.

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Management of manifestations generally associated with the menopausal syndrome—anxiety and tension, vasomotor complaints and hormonal deficiency states.

Contraindications: Women with cancer of breast or genitalia, except inoperable cases, and those with known hypersensitivity to chlordiazepoxide and/or esterified estrogens.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. As with all CNS-acting drugs, caution patients against hazardous occupations requiring complete mental alertness (*e.g.*, operating machinery, driving). Exclude other possible causes of menopausal syndrome manifestations, such as pregnancy. Though physical and psychological dependence have rarely been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage; withdrawal symptoms (including convulsions) similar to those seen with barbiturates have been reported following discontinuance of chlordiazepoxide HCl. Potential benefits of use in pregnancy, lactation or women of childbearing age should be weighed against possible hazards to mother and child. Clinical data inadequate on safety in pregnancy.

Precautions: In elderly and debilitated patients, limit dosage to smallest effective amount of chlordiazepoxide (initially 10 mg or less per day) to preclude ataxia or oversedation; increase gradually as needed and tolerated. Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects—particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in patients with impaired renal or hepatic function. Paradoxical reactions to chlordiazepoxide (*e.g.*, excitement, stimulation and acute rage) have been reported in psychiatric patients. Employ usual precautions in the treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation very rarely reported in patients receiving Librium® (chlordiazepoxide) and oral anticoagulants.

Adverse Reactions: Untoward effects seen with either compound alone may occur with Menrium. With chlordiazepoxide, drowsiness, ataxia and confusion reported in some patients, particularly in the elderly and debilitated; while usually avoided by proper dosage adjustment, these are occasionally observed at lower dosage ranges. Also reported have been a few instances of syncope; isolated occurrences of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido, and occasional reports of blood dyscrasias, including agranulocytosis, jaundice and hepatic dysfunction. Periodic blood counts and liver function tests advisable during protracted treatment. Changes in EEG patterns (low-voltage fast activity) observed during and after chlordiazepoxide treatment.

With estrogens, headache, nausea and vomiting, anorexia, gastrointestinal discomfort, dysuria and urinary frequency, jitteriness, breast engorgement, formation of breast cysts, skin rashes and pruritus occasionally seen. Administration may also be associated with uterine bleeding and/or followed by withdrawal bleeding.

Usual Dosage: One tablet t.i.d. for 21 days, followed by one-week rest periods.

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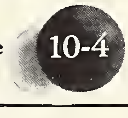
5 mg chlordiazepoxide

0.4 mg water-soluble esterified estrogens

10 mg chlordiazepoxide



0.4 mg water-soluble esterified estrogens

exposed to oxidizing agents such as hydrogen peroxide. Furthermore their red cell survival time are definitely shorter than those in normal persons.

In animals the effects of E deficiency are numerous and quite varied ranging from encephalomalacia in the chick to muscular dystrophy in the monkey.[2] Now we have Ritchie[3] describing the study of seven premature infants with widespread edema and anemia which was hemolytic and associated with thrombocytosis. The edema did not respond to diuretics, the anemia did not respond to iron. A search for the cause of the anemia and edema revealed none until they measured the serum tocopherol levels which turned out to be uniformly low. Administering 75 mg. E daily by mouth separately from other foods restored the infants to normal, within one to three weeks. If, however, iron was given with the tocopherol or if the E was given at the same time as the formula, the vitamin was destroyed in the gastrointestinal tract and recovery did not occur.

It then turned out that the premature infants were fed on a commercial formula consisting of skimmed milk and vegetable oils so that the ratio of E to the polyunsaturated fatty acids were too low. The infants taking breast fed milk showed normal serum E while those with artificial formulas had low serum E. The rise in serum E restored the survival time of the red cell and the authors believe this to be due to the anti-oxidant effect of vitamin E. There can, of course, be other deficiences as ineffective erythropoiesis associated with deficiences such as folic acid, inadequacy of maternal nutrition of fetal nutrition, infant birth weight, body stores of E at birth, and whether the vitamin is administered separately or destroyed when given with other nutriments especially iron and polyunsaturated fats. The edema and vascular damage can be explained if the capillary membrane like that of the erythrocyte undergoes oxidative damage in the absence of E which then permits excessive transudation of fluid resulting in edema formation.

The frequency with which this syndrome is observed will depend on the level of awareness of its existence and the care with which it is sought. It was close observation which led to the detection of six cases of the full syndrome at the San Francisco General Hospital during six months. It is to be expected that in this as in most deficiency states fragments of the syndrome, subtle degrees and subclinical manifestations will also occur. The anemia and edema observed in these infants may be merely the iceberg of a much profounder disturbance as noted above about vitamin B_{12}. Some of the manifestations such as anemia, puffy eyes, firm legs and shiny skin not unusual in premature infants and often called physiologic or characteristics of prematures may prove in many cases to actually represent some form of vitamin E deficiency.

There is need to find answers to several questions posed by Ritchie's observations. One such question is the precise metabolic role of E. Does it serve merely as an excellent anti-oxidant in-vivo, acting as a non-specific protector of membrane-lipid integrity or does it serve also as an essential co-enzyme in a vital biosynthetic pathway as yet undiscovered. It is equally important to determine the extent of the effects of E deficiency in the rapidly growing infant of low birth weight.

There are many biologic variations in the manifestation of the deficiency states in both animals and man. Profound E deficiency in children and adults may produce creatinuria, ceroid deposition in smooth muscle and focal necrosis in striated muscle without a severe hemolytic process. Are these differences due to individual variations in the lipid composition of tissues of the hosts at risk?

All the ramifications of vitamin E deficiences for the growing infant now await further scrutiny. We must learn what other presently unrecognized deficiences afflict these small infants who have been denied not only the total nurture of the womb but also an opportunity to be breast fed, in whom it is never observed. Finally we must not be too complacent about deficiences of vitamins not taking place, merely because people are on a presumed "proper" diet.

L.H.N.

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Foreword

All Medicine looks to the decade of the 1970's with anticipation.

I am firmly convinced that the specialty of Anesthesiology eagerly expects major breakthroughs in this decade, which appear to be signaled by the herculean accomplishments during the 1960's.

Since all the advances in Anesthesiology cannot be elucidated in one short issue, we have attempted to touch those highlights which both affect and should interest the broad spectrum of practice in a medically sophisticated state like Connecticut.

It is fitting that the first view presented in this issue be historical. America made the greatest single contribution to the millenia of medical history—Anesthesia. Anesthesia began in Connecticut with Horace Wells. Following this, we shall view six subjects which I consider to be areas of accomplishment, but more particularly, of promise for the future.

The areas we have chosen to discuss are obstetric and neonatal care, drug interactions, intensive respiratory care, muscle relaxants and the anesthesiologist's relation to law.

Frederick W. Hehre, M.D., *Guest Editor*

Father of Surgical Anesthesia

Dr. Horace Wells

Stevens J. Martin, M.D.

The history of mankind is replete with documented contributions that have affected its continued progress. Perhaps one of the most significant of these has been the clinical introduction of nitrous oxide anesthesia for the elimination of pain during dental and surgical procedures on December 11, 1844 by Doctor Horace Wells.[1-14] As with many other medical discoveries, Dr. Wells was aided by the efforts of others—spanning some five decades—until the day of final decision to have nitrous oxide administered to him first for a dental extraction and then to thousands of his dental patients thereafter. The prompt and widespread acceptance of his procedure constituted a gift to mankind. One is reminded of Louis Pasteur's comment that "the future belongs to those who have done most for suffering humanity."

Dr. Horace Wells was born on January 21, 1815 in Hartford, Vermont.[1,2,4,11] Coming from a family of more than average means and regarded as a "bright boy," he went to school at Amherst, Mass. and then to Walpole, New Hampshire. Being very religious, he almost became a minister. His mind was restless, and inquisitive. He was very sensitive and at times shy. In 1834, at an age of 19, he studied dentistry in Boston under the preceptorship system and gained clinical experience in a dental office. There were no dental colleges available in those days. His professional maturity was rapid in development and his ingenuity in inventing and constructing dental instruments was highly regarded. His desire to teach was strong. He accepted two students, John M. Riggs of Hartford, and William T. Morton of Boston.

Dr. Wells came to Hartford to practice dentistry in November, 1843 after his partnership with Dr. William Thomas Green Morton failed to thrive. This move was providential. On December 10, 1844, Dr. Wells attended a "laughing gas frolic" or demonstration in Hartford at Union Hall which was conducted by a chemist, Mr. Gardner Quincy Colton.[1,12] At this evening session Samuel A. Cooley, a clerk at the largest drug store in Hartford, inhaled the nitrous oxide gas and acted as a "lunatic," "saw an enemy and chased him," hurt himself and then sat down next to Dr. Wells.[4] When the effects of the gas wore off he noticed a "gaping wound below the knee, bleeding, but experienced no pain."[4] It was then that the thought occurred to Dr. Wells to use the nitrous oxide gas in dentistry. The following morning, Dr. Wells visited Mr. Colton and made plans to have a troublesome wisdom tooth extracted by Dr. Riggs, his former student, under the influence of nitrous oxide. This was done on December 11, 1844. After the extraction, Dr. Wells exclaimed, "a new era in tooth pulling. I did not feel it so much as the prick of a pin."[9] Mr. Colton always gave credit to Dr. Wells for suggesting the first practical use of nitrous oxide. Subsequently both Dr. Wells and Mr. Colton administered nitrous oxide to thousands of patients. Mr. Colton formed the Colton Dental Association where he had administered nitrous oxide to over 25,000 cases without a fatality. After the initial success with the gas, Dr. Wells went to Boston to visit his former pupil, Dr. Morton, in the early part of January, 1845. Thru his contacts at the Massachusetts General Hospital, he met Dr. John Warren, the senior surgeon, who permitted a demonstration of nitrous oxide gas for the extraction of a tooth on a volunteer. As the tooth was being withdrawn, the patient made a sharp outcry. This was most likely due to too little gas or too low a concentration. Nevertheless the students promptly jeered, hissed and shouted, "Humbug." Dr. Wells was utterly dejected, left the amphitheater and then to Hartford. What was not known *immediately* was that the patient himself stated he felt *no pain*. Despite the fact that Dr. Wells continued to administer N_2O to many citizens of Hartford, Bishop Brownell, his two daughters, some other 40 citizens of Hartford for dental extraction without pain, Dr. Wells never fully recovered the Boston humiliation. Subsequently, he went to Paris to visit his friend, Dr. C. S. Brewster. After Dr. Wells case was presented to several French learned societies by Dr. Brewster, Dr. Wells was voted an honorary member

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DR. STEVENS J. MARTIN, Director, Department of Anesthesiology, St. Francis Hospital, Hartford, Conn.

of the Paris Medical Society for "having successfully discovered and successfully applied the use of vapors or gases whereby surgical operations could be performed without pain." . . . "and to the last day of time must suffering humanity bless his name." Dr. Wells never read this letter from Dr. Brewster recounting the honor and plaudits of the Paris Medical Society. He died an untimely death in New York City on January 24, 1848 at the age of 33, suffering from the humiliation of Boston and of the rival claims of Dr. Morton and Dr. Jackson for the clinical introduction of general anesthesia.

The discovery and development of inhalation anesthesia has had an interesting if not intriguing past. Four men, Dr. Horace Wells, and Dr. William R. G. Morton, dentists, and Dr. Charles T. Jackson and Dr. Crawford W. Long, physicians, contributed directly or indirectly to "the greatest gift ever made to suffering humanity" (Osler). Claims were made by all four for the discovery. However, the insight, deduction, self experimentation, use on patients and instruction of fellow dentists, made Horace Wells stand out predominantly. A series of testimonials in 1847 by 40 citizens of Hartford of all walks of life, the 50th Anniversary compendium,[1] the voluminous Proceedings of the Centenary Commemorations of Wells Discovery in 1844,[8] the comprehensive presentations and critical analysis by Raper in his book "Man Against Pain," the epic of anesthesia and Archer's presentation on the "Life and Letters of Horace Wells,[11] discoverer of anesthesia," chronologically arranged, all point to Horace Wells as the discoverer of surgical anesthesia. The American Dental Association at its 4th Annual Meeting in Niagara Falls in 1864 adopted the following resolution:

WHEREAS: — — — —

RESOLVED: Therefore be it resolved, by the American Dental Association, that to Horace Wells of Hartford, Connecticut (now deceased) belongs the credit and honor of the introduction of anesthesia in the U.S.A. and we do firmly protest against the injustice done to truth and the memory of Horace Wells, in the effort made during a series of years and especially the last session of Congress, to award the credit to other persons or person." Reaffirmed, 1872.

In the final analysis even the challenges from Sims,[2] Richardson,[3] and others have failed to detract international acclaim for Wells.[8] Horace Wells richly deserves the title of "Father of Surgical Anesthesia."[8]

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Newer Thoughts on Obstetric Anesthesia

Robert Hook, M.D.

Introduction

Changes in maternal physiology during pregnancy and close association of the fetus to the maternal circulation produce a unique anesthetic challenge. The obstetric anesthesiologist must apply current techniques and anesthetic agents to provide anesthesia which is safe for both the mother and fetus. As more precise definitions of maternal and fetal physiological parameters unfold, the responses to obstetrical anesthesia are becoming clarified.

During labor, each uterine contraction subjects the fetus to repetitive stress. The individual and cumulative effects on the fetus can both be measured and used in the clinical management of the patient in labor.[1]

Fetal Monitoring

One of the most exciting developments in recent years has been the use of fetal electrocardiography and intrauterine pressure measurements to monitor the well-being of the fetus and the progress of labor. Inexpensive clinical fetal monitors (Fig. I) are commercially available for labor and delivery room use. Individual monitors may be displayed on multiple channel central monitoring systems. Extensive clinical descriptions of fetal heart rate patterns by Hon and Caldeyro-Barcia, have defined almost every clinical situation.[1,2,3] Correlations of fetal heart patterns with the acid base status of the fetus measured by fetal scalp blood samples correlate well, although in later time, with electrocardiographic patterns of fetal distress.[4,5,6] The obvious lesson of electronic and biochemical monitoring emphasizes the inadequacy of previous criteria of fetal distress. Changes in fetal heart rate indicate that fetal distress cannot be verified by intermittant auscultation of fetal heart sounds. When the fetus is subjected to increased risk by maternal disease, for example, diabetes and preeclampsia, electronic fetal monitoring permits earlier decisions to be made concerning obstetric and anesthesiologic management. In relative cephalopelvic disproportion, fetal electrocardiography and intrauterine pressure measurement determine both the quality of the labor and fetal welfare. The same is true during elective induction of labor when progress of labor in terms of effective uterine contractions without compromise of the fetus can be followed.

Fetal electrocardiography has wide application as a research tool. Effects of drugs in the clinical management on the labor and the welfare of the fetus can be determined precisely. It is presently possible to state categorically that even the present methods of fetal monitoring will be required in the evaluation of any new drug which enters the fetal circulation. Electronic measurement of minute changes within the fetal electrocardiogram itself associated with drug induced changes in the fetal autonomic nervous system are presently being done. Hon has described the R-R interval of the fetal electrocardiogram as a measure of the integrity of the fetal autonomic nervous system. Variations in fetal maturity as well as the effects of placental transmission of opiates, barbiturates, tranquilizers, belladonna alkaloids and local anesthetics produces changes in the conformation of the R-R interval.[7]

General Anesthetics

Over four million obstetrical anesthetics are administered in this country annually. More than half are given by personnel with minimal training in anesthesia and fewer by anesthesiologists especially interested in obstetrical anesthesia, although agents used in obstetrical anesthesia include the most potent drugs known.[8,9]

Knowledge of the mechanisms of uptake, distribution, and elimination of general anesthetic agents provides foundation for their rational use in obstetrics.[10] Production of anesthesia depends upon delivery of the anesthetic to the brain. With inhalation agents, this depends on intact function of the lungs, heart, and circulation.[11] Many variables affect the rate of delivery and the final concentration of anesthetic to the brain. The speed at which an anesthetic accumulates in the arterial blood depends upon the balance between rate of addition and rate of removal. With normal pulmonary and cardiovascular function, addition is controlled by the inspired gas concentration.[12] Rapid removal of the agent occurs initially by redistribution from the blood into vessel-rich tissues. Thiopental owes its

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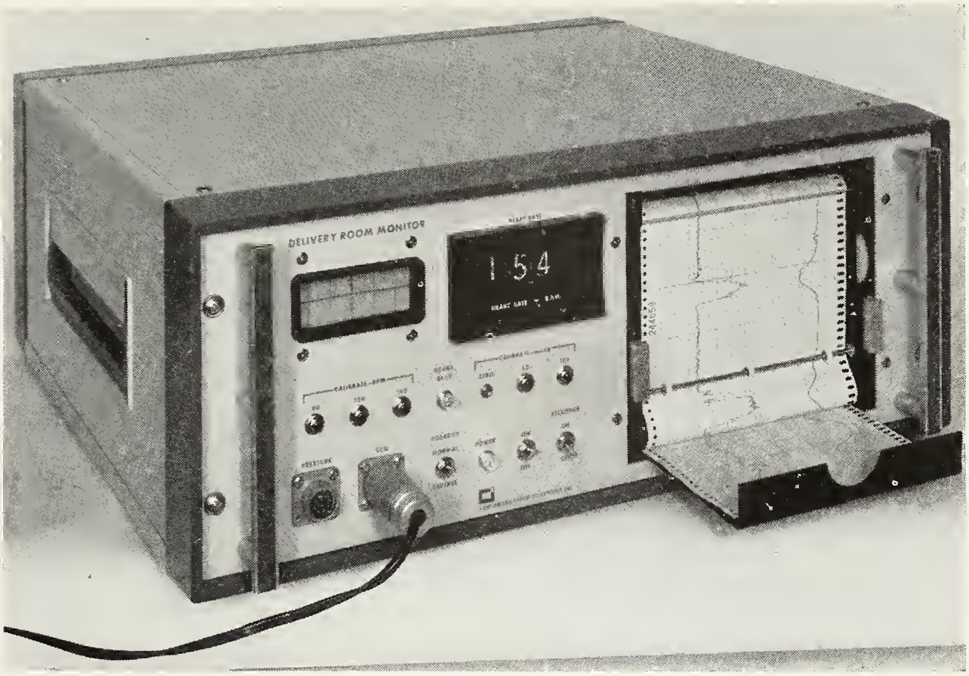

Figure 1

Clinical monitor for use during labor and in the Delivery Room. The automatic paper drive runs at 3 cms. perminute; and displays the fetal heart rate on the left and intraamniotic fluid pressure on the right. The fetal heart rate input is from a bipolar scalp electrode and amniotic fluid pressure input is from a transcervical catheter.

—Courtesy Corometrics Medical Systems

"ultra short" action to redistribution and not to rapid metabolic degradation. With inhalation agents, the rate of removal from the blood decreases as the tissues become saturated and the inspired concentration necessary to maintain a given arterial blood level decreases.[13]

Situations exist in obstetrical practice when general anesthesia is necessary. Emergency caesarean section when conduction anesthesia is impossible, or when extreme relaxation of the uterus is necessary, as for version and extraction, are two examples, and, precautions which minimize the risk of maternal aspiration are indicated.[14] Awake endotracheal intubation is the technique of choice, but is seldom possible in the emotional and painful obstetrical situation. Rapid or "crash" induction and rapid endotracheal intubation is effective, but does expose the patient to the risk of obstruction and aspiration. It is our opinion that the use of general anesthesia for the normal vaginal delivery represents an unnecessary risk in terms of fetal and maternal morbidity and mortality. Pregnant women at term have surprising amounts of gastric contents. Gastric emptying is slowed during labor and anatomical displacement of the stomach by the gravid uterus produces pocketing of gastric contents.[15]

General anesthetic agents pass through the placenta rapidly.[16] The effect on the fetus depends on potency, solubility in body tissues, concentration, and the length of exposure. Cyclopropane is potent, non-soluble, and provides rapid induction and appears in the fetal circulation within minutes. Cardio-respiratory depression of the fetus increases after the first 3-5 minutes of maternal exposure to anesthetic levels. Five percent concentrations of cyclopropane in oxygen provide *analgesia* without undue depression of maternal laryngeal reflexes and have no apparent effect on the fetus even with prolonged maternal exposure.

Halothane is a potent, soluble vapor which, when used with nitrous oxide and oxygen provides a rapid induction and causes fetal depression. Halothane produces profound relaxation of the uterus, and is the agent of choice in obstetrical situations requiring uterine relaxation for intrauterine manipulation.

Methoxyflurane is a potent soluble agent with a prolonged induction time and cannot produce general anesthesia without transfer of large amounts of agent to the fetus. Methoxyflurane provides analgesia when administered in low concentration, with nitrous oxide, a soluble gas of low potency.

Thiopental, given to the mother in doses of 300 mg or less intravenously, has little effect on the mature fetus, and levels in the umbilical arteries have been found to be clinically insignificant.[17] Thiopental is absorbed from umbilical venous blood into the fetal liver, and, relatively little thiopental reaches the fetal cerebral circulation. More than 300 mg saturates this protective mechanism, and raises arterial levels of thiopental producing fetal depression.[17,18]

The highly ionized, non-lipid soluble muscle relaxants, succinylcholine and curare, do not pass the placenta and usual clinical doses have little effect on the fetus.[16]

For uncomplicated vaginal delivery, inhalation analgesia with nitrous oxide-methoxyflurane and oxygen combined with bilateral pudendal nerve block or local infiltration of the perineum is probably the most effective and safe technique for both mother and baby in our opinion.

Regional Analgesia

In the obstetric patient regional analgesia is considered a safer approach by many anesthesiologists. Conduction anesthesia, when maternal hypotension is avoided, has less effect on the fetus than general anesthesia. Adverse effects on the fetus result from maternal hypotension and decreased placental blood flow. Local anesthetics cross the placenta barrier rapidly and have effect on the fetal electrocardiogram, but little apparent clinical effect on the fetus.[7] Studies of local anesthetics in mixed arterial venous umbilical blood samples at deliveries when peridural anesthesia was used have shown fetal levels to be lower than maternal levels indicating a placental gradient.[19,7]

Venous blood levels of local anesthetic drugs containing epinephrine reach peak 15-20 minutes after injection into the peridural space.[20] Low dosage schedule of local anesthetics for peridural anesthesia used in this clinic have not been associated with toxicity to either mother or fetus.[21] High levels can occur if the drug is inadvertantly injected into a blood vessel.[22] Local anesthetics have direct depressant action on vascular smooth muscle, as well as on the heart, the magnitude being proportional to the blood level of the drug. Local anesthetics also cause fall in peripheral resistance.

Low spinal anesthesia, or saddle block, is an effective technique for vaginal delivery when the application of low forceps is desirable. Lumbar peridural and caudal analgesia provide continuous analgesia from first stage and through episiotomy repair. Caudal analgesia requires more milligrams of local anesthetic to attain the same sensory levels as does lumbar peridural anesthesia. This is disadvantageous from the standpoint of maternal toxicity, since levels at the tenth thoracic segment are necessary to abolish painful uterine contractions. Insertion of a needle into the caudal canal when the fetal head is at low station has resulted in inadvertant injection into the fetal head.[23]

Maternal complications of regional analgesia are hypotension, drug overdose, and inadvertant dural puncture resulting in total subarachnoid block. Hypotension results from combination of sympathetic blockade, compression of the inferior vena cava in the supine position, and extracellular fluid volume depletion. The magnitude of hypotension can be lessened by confining the block to levels necessary to block painful contractions. Lateral position and replacement of depleted extracellular fluid volume with balanced electrolyte solution are also beneficial.[24,25]

Excessively high block, or severe extracellular fluid depletion, may necessitate the use of vasopressors. Vapopressors which increase blood pressure by increasing cardiac output, for example, ephedrine, are preferrable[26] to peripheral vasoconstrictors. We consider the use of prophylactic vasopressors to be unnecessary. Recent studies by Marx indicate that the single most important factor in the prevention of hypotension is replacement of extracellular fluid volume. Prophylactic vasopressors alone or in combination with fluid replacement were shown to produce results no better than those provided by fluid replacement alone.[27] Peripheral arteriolar vasoconstrictors have been shown to cause fetal hypoxia from reduced placental blood flow.

Maternal hypotension may be caused by relative or absolute overdose of local anesthetic drugs, and is usually accompanied by signs of central nervous system toxicity. Severe tachycardia may result from intravascular injection of an epinephrine-containing drug. Local anesthetic overdose is treated with position, oxygen, artificial ventilation, and finally vasopressors.

Inadvertant subarachnoid injection of large amounts of local anesthetic drugs used in extradural anesthesia can result in massive spinal block, treatment is with artificial ventilation, position and vasopressors as indicated.

Caesarean Section

Elective caesarean section when speed of induction is not critical is best managed with regional anesthesia, in our opinion. Levels to T-4 are desirable to provide patient comfort without the use of other drugs. It has been shown by Marx et al.[27] that infusion of 800-1000 cc's of balanced electrolyte solutions decreases the incidence and magnitude of hypotension. The decreased size of the maternal subarachnoid space in pregnancy necessitates the use of smaller doses of local anesthetic drug for the production of this level.[24] In our practice we use not more than 10 mgs of tetracaine usually without epinephrine. Peridural anesthesia for elective caesarean section is common. It is often assumed that hypotension with peridural anesthesia is less frequent than with spinal. Since the level of sympathetic block seems to coincide with the sensory level in peridural anesthesia, one expects a lower incidence of hypotension.[28] With levels at T-4, however, this difference would probably not be apparent.

When general anesthesia is necessary, the hazards of gastric contents must be minimized by awake or rapid endotracheal intubation. Thiopental, nitrous oxide, succinylcholine is preferred with the induction dose of thiopental 300 mg or less, and that no more thiopental be given before clamping the cord. During general anesthesia the induction-to-delivery time should be as short as possible to minimize anesthetic depressant effect on the fetus.[27] With nitrous oxide a significant increase in the number of sleepy babies occurs when induction-to-delivery interval exceeds 20 minutes. With potent agents as cyclopropane, the baby should be delivered as rapidly as convenient after induction of anesthesia.

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SHAKESPEARE AND MEDICINE

Observance in 1964 of the 400th anniversary of the birth of William Shakespeare (1564-1616) has been marked by numerous articles commenting on the hundreds of references in his works to diseases of mankind. Physicians have found his writings entertaining literature as well as informative medically.

Shakespeare's plays are full of medical puns and precise and clinical descriptions. Considering medical knowledge in his time, he accurately described syphilis, pox, typhoid, malaria, dropsy, jaundice, emphysema, toxemia of pregnancy, gallstones, death by snakebite, arsenical poisoning, and many other situations.

William Harvey in 1619 described for the first time the mechanics of the heart and circulation of blood. Years, before, Shakespeare in Coriolanus wrote:

> I send it through the rivers of your blood,
> Even to the court, the heart,—to the set o' the brain;
> And, through the cranks and offices of man,
> The strongest nerves and small inferior veins:
> *Coriolanus,* act I, scene I

Shakespeare showed remarkable knowledge of insanity. There is scarcely a form of mental disorder to which he had not alluded, pointed out its cause, or described the method of treatment. His views were far in advance of the times.

This has led some commentators to conclude that he may have studied medicine between 1584 and 1592, an unknown period in his life. Most Shakespearean authorities, however, believe the bard merely was well informed since medical knowledge by learned laymen was commonplace in those days.—Mirt, J. A.: "Medical Pathfinders on Postage Stamps," an exhibit.

The First Sixty Minutes of Life

Leandro Cordero, Jr., M.D.

Introduction

During the crucial first minutes of life, the human newborn, whether vigorous or depressed, may receive help from personnel of many medical disciplines (i.e.: obstetricians, pediatricians, general practitioners, anesthesiologists, anesthetists, nurses, midwives, etc.). Although there are many standards for routine delivery room care,[1-3] dissimilar experience and training are reflected by different approaches and practices.

The increasing knowledge of the physiologic adjustments of the first hour of life prompts us to review some old concepts and routines. In order to provide continuous and sensible support for the newly born we should expand our concern beyond the establishment of vigorous respiration and a steady heart rate.

Routine procedures and resuscitation techniques have been extensively covered[1-3] elsewhere; therefore, I will comment on those events of extrauterine life, the understanding of which might help to provide better and more intelligent neonatal care.

Establishment of a Clear Airway

The vigorous infant delivered vaginally usually only needs suctioning of the nasopharynx with a bulb syringe when the head is delivered. In the crib, another gentle bulb suction is enough to eliminate any excess mucus, and/or amniotic fluid. Prolonged and energetic suctioning with a nasogastric tube attached to a DeLee trap is not only unnecessary but can be dangerous. A small catheter introduced blindly, may reach the trachea or larynx and may trigger powerful vagal responses that not only will produce bradycardia, but may also produce apnea.

We have monitored fetal heart rate and fetal electrocardiograms during labor and have observed the neonate during the first hour of life. Continuous neonatal electrocardiograms, instantaneous neonatal heart rate and serial arterial blood gas samples were taken during the first sixty minutes of life in a large research population. The records of 85 infants were studied in retrospect to assess the incidence of neonatal bradycardia during nasopharyngeal suction. Seven of 42 infants suctioned with a catheter through the nose or the mouth during the first two minutes of life developed significant bradycardia, and four suffered concomitant apnea. None of these patients had previous evidence of fetal distress and their arterial cord biochemistries were comparable with those of vigorous babies. Five infants had one minute Apgar scores better than 8. Bradycardia was not observed in the forty-three babies suctioned with a bulb syringe.[4]

Examples of neonatal bradycardia associated with nasopharyngeal suctioning with a catheter are shown in Figure 1. The tracings displayed belong to two full-term infants born vaginally who showed no fetal distress during labor.

The real incidence of this iatrogenic bradycardia is unknown at the present, but it is probably common since 40 percent of babies in this hospital who scored 9-9 on the Apgar method receive DeLee trap suctioning.

The presence of meconium stained fluid or thick mucus, especially in depressed infants, requires more vigorous clearing of the upper airway. The use of the catheter and DeLee trap under direct vision may be required prior to endotracheal intubation. Only the trachea and main bronchi can be cleared by this method; therefore, there is no justification in delaying further the onset of ventilation.

Gastric Aspiration

After the first five minutes of life, the gentle passage of a nasogastric tube to obtain gastric aspirates should not produce untoward vagal responses and provides valuable information regarding the patency of the upper airway and upper gastrointestinal tract.

Babies born by cesarean section, in particular offspring of diabetic mothers, may have more gastric contents than infants born vaginally.[5] Evidence that removal of such gastric contents is beneficial is

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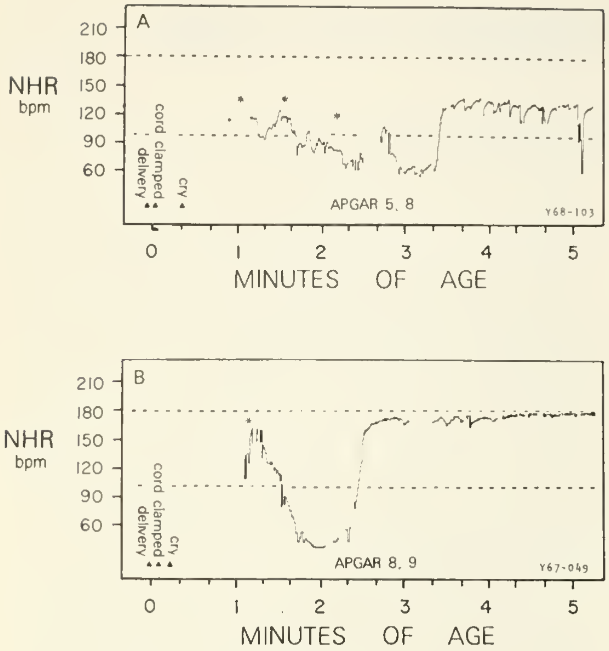

Figure 1

Neonatal heart rate pattern in infants who developed bradycardia associated with blind nasopharyngeal stimulation.

* Beginning of DeLee trap suctioning.

+ NHR = Neonatal heart rate; bpm = beats per minute.

still lacking, but premature or depressed babies may regurgitate and aspirate undesirable material.

The presence of leukocytes and/or bacteria in smears of gastric aspirates represents an aid to detection of intrauterine infections. Bacteriologic cultures may identify the responsible pathogen in neonatal sepsis.[6-7]

Temperature Control

At the environmental temperature of most delivery rooms (26°C), the newborn infant suffers serious heat loss during the first few minutes of life. Body temperature is a balance between heat loss and heat production, and a wet neonate with a large surface area may lose 2 to 3° C. of temperature during the first five minutes of extrauterine life.[8]

In small newborns the ability to limit heat loss is small, but the capacity to increase heat production, as reflected by rises in oxygen consumption, is large.[9] The smaller the body size and thermal insulation, the narrower is the range of environmental temperature over which that heat balance is maintained.[8]

Maintenance of body temperature immediately after birth exerts a beneficial effect upon the rate of recovery from metabolic acidosis. Vigorous infants left uncovered at room temperature develop a significant metabolic acidosis, but by increasing CO_2 elimination they are able to achieve and maintain a relatively normal pH. Depressed infants suffer a more pronounced and prolonged fall in temperature[11] and seem unable to compensate the persistent metabolic acidosis.[8]

Routine delivery room and nursery techniques alter significantly the maintenance of body temperature. Newborns with the same temperature at birth responded differently when exposed to cooling; for example, those who were routinely managed in the delivery room and bathed on admission to the nursery exhibited mean rectal temperatures of 34.5° C. at one hour of age, but infants not bathed, reached a low mean temperature of 35°C. Those placed in an incubator and dried immediately after birth had a mean temperature of 36° C. on admission to the nursery. More significantly those babies kept in the incubator reached normal rectal temperature of 36.5° C. within three hours whereas it was not achieved in the other two groups until eight hours of age.[12]

In newborn lambs delivered by cesarean section and kept in warm saline with intact umbilical circulation, cooling of the skin, especially the face, will start rhythmic changes of intraesophageal pressures.[9] Newborn guinea pigs asphyxiated after cooling or cooled during asphyxiation showed prolonged survival time.[13] However, these animal experiments provide valuable information which should be cautiously interpreted if one wishes to derive clinical policies that will decrease mortality as well as irreversible sequelae.

Under normal circumstances, the stimulus of falling skin and rectal temperature at birth contributes to the onset of breathing. Depressed or asphyxiated infants benefit from early prevention and correction of further heat losses.

Immediately after birth the newborn should be dried and placed on any available warming device. Commonly used air convection systems do not allow easy access to the baby and do not prevent heat loss by radiation. To be effective, they should be kept closed continuously. Open or semiclosed radiant units are more efficient in maintaining skin and body temperature if insulating clothing and vernix have been removed. Servocontrolled units can be set to a constant skin temperature and skin sensors can be applied anywhere, preferably over the liver.[15]

Continuous reading of skin temperature provides a valuable guide in the delivery room since changes in skin temperature precede those deep within the body. As cooling progresses the infant increases his metabolism in order to generate heat thus delaying the fall in rectal temperature.

Acidosis

Labor and delivery, even under normal circumstances, produce an acid-base imbalance in the neonate which takes minutes and sometimes hours to correct spontaneously.[16,17,18] Depressed infants usually have a more profound and prolonged metabolic and respiratory acidosis (Table 1). Clinical evaluation by Apgar score correlates well with umbilical arterial pH except in cases of drug depression.[16,20] Babies with high Apgar scores can suffer severe acidosis which may be clinically unrecognized and remain uncorrected for hours. Figure 2 shows the biochemical adjustment of 20 babies who scored 8 or more at 1 and 5 minutes in the Apgar scale. Those who had an arterial cord pH equal to or greater than 7.25 recovered faster than those who were acidotic at birth. All patients had similar birth weight and none had drug depression. Five of the ten infants in the more acidotic group showed biophysical and biochemical evidence of fetal distress.

Vigorous full-term infants will overcome the effects of unrecognized acidosis but high risk babies, i.e., prematures, post-matures, offspring of diabetic mothers, etc., may suffer immediate or late consequences.

Asphyxia

The ability of the newborn animal to survive asphyxia depends on high cardiac glycogen concentration and the ability to obtain energy from anaerobic glycolysis.[9]

Studies of asphyxiated rhesus monkeys have shown that the infusion of base and glucose prevents bradycardia and that when given simultaneously with artificial ventilation, recovery of animals was significantly facilitated.[21] Acidosis should be immediately corrected in babies who required prolonged and intensive resuscitation.[3] The potential hazards of rapid correction of acidosis by intravenous infusions[22] must be weighed with the benefits of rapid resuscitation.

Information regarding dangers of hepatic damage after umbilical infusion of THAM or sodium bicarbonate is still conflicting.[23,24] Under stressful conditions of the delivery room 3 mEq of sodium bicarbonate per Kg of body weight, undiluted or, preferably, diluted to 1/3 in ten percent dextrose may be administered over a one minute period as resuscitation progresses. It may be repeated if no clinical response is obtained in a few minutes. The infusion should be given through an umbilical arterial or venous catheter, but may be given with a hypodermic needle into the umbilical vein.

In depressed infants, arterial, arterialized capillary or even venous blood should be taken every 15 to 20 minutes to monitor biochemical recovery for a period of at least one hour. Glycogen stores are rapidly depleted in asphyxiated infants and severe hypoglycemia may occur during the first few hours of life, therefore, it is advisable to obtain serial blood sugar determinations.

A baby who has suffered intrauterine or neonatal asphyxia even if he looks vigorous, should be monitored as carefully as those who had been depressed because he may also have unrecognized acidosis, hypoglycemia or hypothermia·

Summary

Physicians and nurses responsible for delivery room care of the newly born must be aware of the physiologic adjustments of the first hour of life. Concern for the infant's well-being should go be-

TABLE 1

ACID-BASE BALANCE IN NORMAL AND DEPRESSED INFANTS*

(Yale-New Haven Hospital 1967-1969)

No. of Infants	*Labor and Delivery*	*Average Apgar Score*		*pH*		*pO_2 mmHg*		*pCO_2 mmHg*		*Base Deficit (mEq/1)*	
		1 min.	*5 min.*	*x*	*SEM*	*x*	*SEM*	*x*	*SEM*	*x*	*SEM*
11	Documented Fetal Distress	1.1	5.5	7.09	±0.01	12.6	±2.2	61.4	±3.2	−13.6	±0.7
21	Uneventful	8.7	9.0	7.20	±0.01	21.9	±1.8	48.3	±1.7	−9.9	+0.7

* Arterial sample taken from umbilical cord.

x Mean value.

SEM Standard error of the mean.

yond the establishment of vigorous respiration and stable circulation.

Blind suctioning of the nasopharynx with a catheter and a DeLee trap in vigorous infants is unnecessary and may lead to severe cardiac and respiratory arrythmias. Gastric aspiration done after the newborn has stabilized may provide valuable information regarding intrauterine infections, and patency of the upper respiratory and gastrointestinal tract.

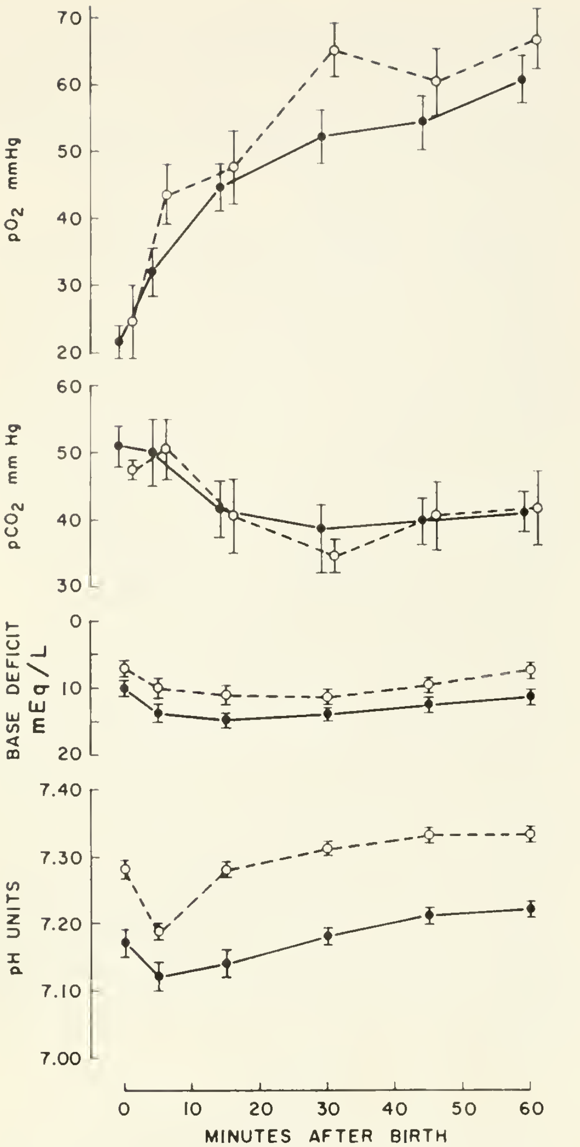

Figure 2

Biochemical adjustments of vigorous infants during the first hour of life.*

- • Mean values and standard error of the mean, 10 infants with cord pH <7.25.
- ° Mean value and standard error of the mean, 10 infants with cord pH $\geqslant 7.25$.
- * Blood sample taken from the umbilical artery.

Resuscitation of a newborn is not complete until the acid-base imbalance has been corrected. Intrapartum events may produce prolonged and severe acidosis in apparently healthy infants.

Cold injury of the neonate is the most common pitfall of delivery room care that can be prevented by appropriate techniques and careful monitoring of skin temperature.

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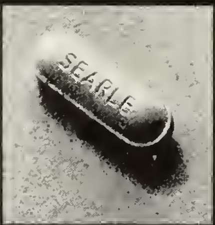

Pro-Banthīne P.A. 30 mg.
propantheline bromide
in time-release form

Pro-Banthīne 7½ mg.
propantheline bromide
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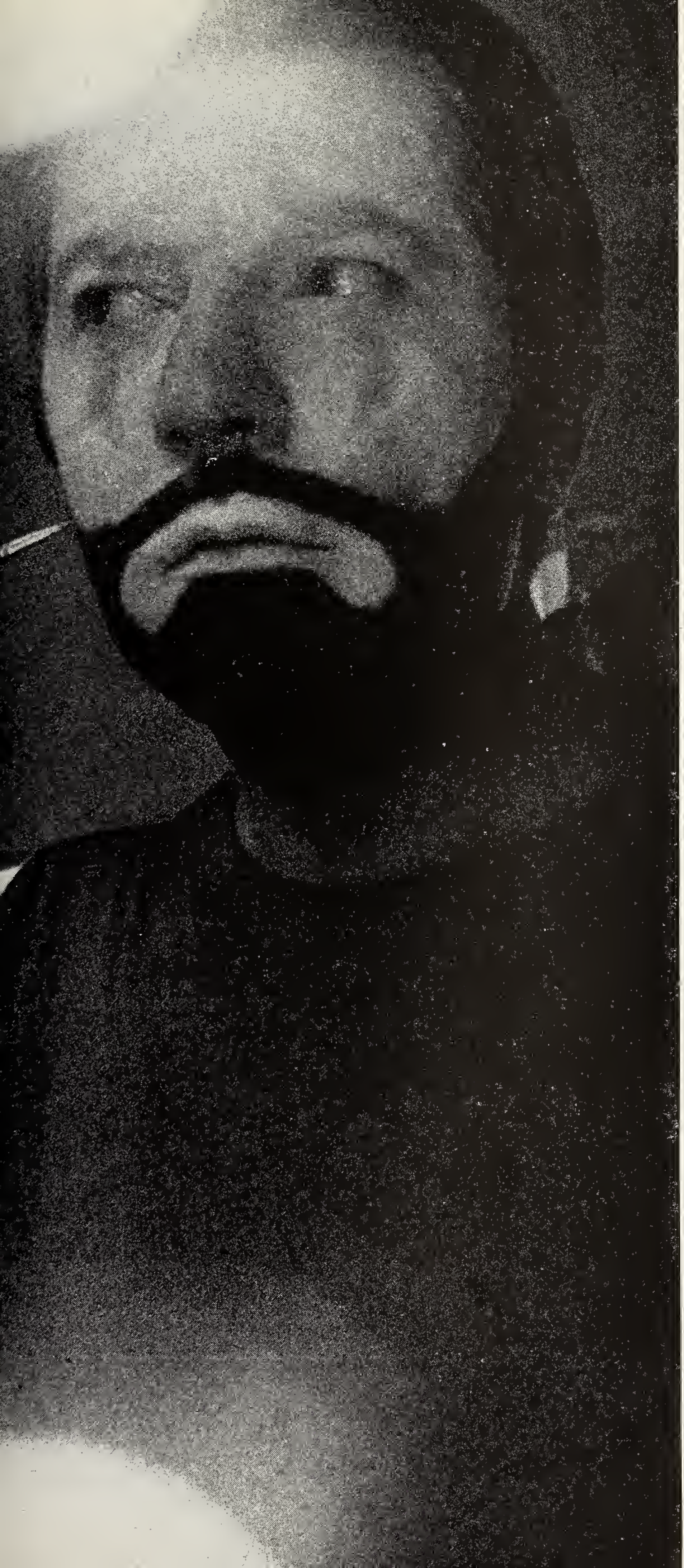

Pro·Banthīne®
(propantheline bromide)

Indications: Peptic ulcer, gastroenteritis, pylorospasm, biliary dyskinesia, functional hypermotility and irritable colon.
Contraindications: Glaucoma, severe cardiac disease.
Precautions: Since varying degrees of urinary hesitancy may occur in elderly men with prostatic hypertrophy, this should be watched for in such patients until they have gained some experience with the drug. Although never reported, theoretically a curare-like action may occur with possible loss of voluntary muscle control. Such patients should receive prompt and continuing artificial respiration until the drug effect has been exhausted.
Side Effects: The more common side effects, in order of incidence, are xerostomia, mydriasis, hesitancy of urination and gastric fullness.
Dosage: The maximal tolerated dosage is usually the most effective. For most adult patients this will be four to six 15-mg. tablets daily in divided doses. In severe conditions as many as two tablets four to six times daily may be required. Pro-Banthīne is supplied as tablets of 15 mg., as prolonged-acting tablets of 30 mg. and, for parenteral use, as serum-type vials of 30 mg. The parenteral dose should be adjusted to the patient's requirement and may be up to 30 mg. or more every six hours, intramuscularly or intravenously.

Pro·Banthīne® 15 mg.
(propantheline bromide)
with
Dartal® 5 mg.
(thiopropazate dihydrochloride)
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Contraindications: Glaucoma, severe cardiac disease.
Warnings: Pro-Banthīne with Dartal should not be administered to patients who are under the influence of barbiturates, alcohol or narcotics. The drug should be administered cautiously to epileptic patients or those in depressed states, patients with liver disease and to pregnant women. Hypersensitivity to Dartal may occur rarely in patients with known sensitivity to similar drugs.
Side Effects: Dryness of the mouth, mydriasis, hesitancy of urination; less commonly extrapyramidal (restlessness, dystonia and signs of pseudoparkinsonism such as muscular rigidity, fixed facies, tremor, ataxia, festinant gait and drooling), parasympatholytic (blurred vision, xerostomia, hypotension, nasal congestion and constipation) and curare-like (loss of control of voluntary muscles, particularly the muscles of respiration) reactions. Rarely, leukopenia or allergic purpura. A generalized erythematous skin reaction may occur. Side effects characteristic of phenothiazines such as grand mal convulsions, altered cerebrospinal proteins, cerebral edema, potentiation of the effects of atropine, heat or phosphorus insecticides, autonomic reactions, endocrine disturbances, reversed epinephrine effect, hyperpyrexia or pigmentary retinopathy may theoretically occur but have not been reported with Dartal. Severe hypotension following recommended doses occurs more commonly in patients who are also afflicted by other medical disorders such as mitral insufficiency or pheochromocytoma, and particular attention should be paid to such a possibility although this has not been observed with Dartal.
Adult Dosage: One tablet three times a day.

Pro·Banthīne® 15 mg.
(propantheline bromide)
with
Phenobarbital 15 mg.
Warning: May be habit-forming.
For *Indications, Contraindications, Precautions, Side Effects* and *Dosage* see Pro-Banthīne. In addition, phenobarbital should be administered with caution to patients with liver disease, mental disturbances or a significant degree of hypoxia.

Pro·Banthīne P.A.®
prolonged acting brand of propantheline bromide
For *Indications, Contraindications, Precautions* and *Side Effects* see Pro-Banthīne.
Dosage Form: Capsule-shaped, compression-coated, peach tablets of 30 mg. for oral use.
Dosage: The recommended initial dosage is one tablet in the morning and one at night.

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Interactions Between Certain Drugs Used Preoperatively and Anesthetic Agents

John C. Daniels, M.D.

A wide variety of commonly used drugs interact with anesthetic agents either directly or as a result of specific alterations which they create in different body systems. These interactions may be detrimental to the maintenance of homeostasis during anesthesia, surgery, or in the early post-operative period. The use of three classes of drugs has become increasingly frequent: psychotropic drugs for treatment of anxiety, agitation and depression; oral diuretics for treatment of fluid retention and mild hypertension; and, anticholinesterases for treatment of glaucoma. This paper will discuss interactions between these drugs, anesthetic agents, and indicated therapy.

Ophthalmic Anticholinesterases—Echothiophate

The organo-phosphorus compound echothiophate (Phospholine Iodide) is an irreversible inhibitor of both red cell (true) and plasma (pseudo) cholinesterase. The ophthalmic form, used in the management of chronic glaucoma and accommodative esotropia, when introduced into the conjunctival sac, produces intense prolonged miosis. Systemic absorption decreases pseudo-cholinesterase activity almost immediately, with maximal depression reached after three to four weeks of therapy. Levels of less than 5% of normal pseudocholinesterase activity have been reported.[1] Intense cholinergic stimulation (diarrhea, vomiting, intestinal colic, salivation and perspiration) and significant depression of true cholinesterase activity have also been reported. [2]

The short duration of action of the skeletal muscle relaxant succinylcholine is due to rapid hydrolysis by pseudocholinesterase. Reduction of pseudocholinesterase activity may impair the hydrolysis of succinylcholine and produce prolonged apnea. Cavallaro, et al. studied this problem in human volunteers. The duration of muscular block produced by succinylcholine, 20 to 60 mg I.V., was determined before and after the administration of oral echothiophate. Pseudocholinesterase activity was depressed an average of 79% (range 51-100%) after echothiophate, while the duration of muscular block increased an average of 22.5% (range 14.3-339%). The authors concluded that in the usual dosage range of succinylcholine, patients maintained on echothiophate may have prolonged apnea, but not to alarming proportions.[3] Pantuck observed a 12 year old boy with congenital glaucoma who had received echothiophate for nine months. Succinylcholine, 20 mg I.V., produced depression of muscle response to ulnar nerve stimulation for 15 minutes. Pseudocholinesterase activity was 30% of normal, with normal flouride and dibucaine numbers.[4]

Conversely, Gesztes reported apnea of five and one-half hours duration following the administration of succinylcholine, 250 mg I.V., over a one hour period, to a 72 year old woman, operated upon for severe abdominal cramps, vomiting, diarrhea and profuse sweating. Surgery revealed thickened wall of terminal ileum, of unknown etiology, but no intestinal obstruction. Post-operatively, the pseudocholinesterase activity was less than 30% of normal, with normal Michel and dibucaine numbers. In retrospect, the patient's symptoms were manifestations of cholinergic stimulation secondary to true cholinesterase depression, and the prolonged apnea secondary to pseudocholinesterase depression combined with the administration of a relatively large dose of succinylcholine.[5]

Echothiophate must be discontinued at least four weeks prior to surgery for pseudocholinesterase levels to return to normal prior to surgery.[1] If surgery is emergent, the use of succinylcholine should be limited to facilitation of intubation, and the total dose kept minimal.

Thiazide Diuretics

The thiazide diuretics are compounds, structurally related to carbonic anhydrase inhibitors and sulfonamide antibiotics, which are effective when administered orally.[6] They interfere with sodium

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reabsorption either in the distal loop of Henle or in the proximal convoluted tubule.[7] They exert specific relaxing effect on smooth muscle,[6] and are used, alone or with anti-hypertensive drugs, to treat mild, benign hypertension. In addition to increased sodium excretion, thiazides, by unknown mechanisms, cause continuous, significant potassium loss. Potassium depletion can result in two adverse effects during anesthesia: 1) the development of prolonged apnea following the use of muscle relaxants and 2) the development of cardiac arrythmias in patients receiving digitalis.

The magnitude of the resting muscle membrane potential (RMP) and the motor end-plate potential bears direct relation to the ratio of potassium inside and outside the cell. This ratio (K+ inside/K+ outside) in milliequivalents is approximately 30 and results in a RMP of −90 millivolts.[8] A decrease in K+ outside relative to K+ inside (hypokalemia) causes the RMP to become more negative, and hyperpolarizes the cell membrane. The membrane is then more resistant to the depolarizing effects of acetylcholine and succinylcholine, and more sensitive to the action of non-depolarizing relaxants.[8] The development of desensitization, or phase II block, occurs more rapidly, and with greater frequency after succinylcholine administration.[9]

Patients receiving thiazide diuretics (as well as those with primary aldosteronism, chronic diarrhea and chronic glomerulonephritis) have deficits in both intracellular and extracellular potassium.[8] If intra- and extra-cellular potassium fall in constant ratio, so that the RMP remains approximately −90 millivolts, the response to relaxant drugs remains unchanged. Oldfield has reported the case of a surgical patient with a potassium of 1.4 meg/L but with a normal response to curare.[10]

The danger of combined potassium deficit lies in its instability. Relatively small shifts of potassium intracellularly, hemodilution with potassium deficient solutions, or diuresis may produce hypokalemia such that the effects of non-depolarizing drugs are greatly enhanced.[8,11,12] Treatment consists of the administration of intravenous potassium. Neostigmine-resistant curarization in hypokalemic patients has been reported.[13] Feldman states that these patients may have been suffering from metabolic and/or respiratory acidosis. Such patients can develop a picture identical with persistent or recurrent curarization that responds not to neostigmine or potassium, but to alkalinizing agents such as sodium bicarbonate.[14]

Electrocardiographic evidence of hypokalemia occurs when plasma potassium values reach 2.2 to 3.0 meq/L.[15] The classic changes involve the repolarization phase: loss of the T wave, ST depression greater than one millimeter, and a U wave greater than three millimeters. With higher values for plasma potassium, one may see an upright T wave of low amplitude, minimal or no ST depression, and U waves not only of lower amplitude, but also fused with and indistinguishable from the T wave.[15,16] Lack of correlation between plasma potassium concentration and the electrocardiograph pattern has been frequently observed. Libretti and others have observed better correlation between intracellular potassium and electrocardiographic changes.[16] According to Primzmetal, et al. the alterations of the repolarization phase depend upon the gradient between intracellular and extracellular potassium concentration rather than their actual values.[17]

Digitalis interferes with the active transport of sodium and potassium across the cardiac cell membrane, presumably by displacing potassium from its "carrier" on the outside of the cell membrane. The net effect is loss of intracellular potassium, a gain in intracellular sodium, and a rise in the resting membrane potential toward the threshold of spontaneous depolarization. (−60 millivolts) The closer the RMP approaches threshold, the more excitable is the cell. Since the digitalis glycoside displacement of potassium is competitive, any factor decreasing extracellular potassium increases digitalis-induced inhibition of potassium transport. The potential result is digitalis toxicity and cardiac arrythmia. Increasing extracellular potassium displaces digitalis from the "carrier", permits normal electrolyte transport, and reduces the potential for arrythmia.[18]

Hypokalemia alone rarely produces arrythmias, although ventricular ectopic beats and ventricular tachycardia have been reported.[19,20] In combination with digitalis, the arrythmias produced are directly related to digitalis toxicity: paroxysmal atrial tachycardia with A-V block, nodal and A-V junctional tachycardia, A-V dissociation, ventricular ectopic beats, and ventricular tachycardia and fibrillation.[20] In anesthetized patients receiving digitalis and thiazide diuretics preoperatively, normal values for extracellular potassium are no guarantee that the patient is not potassium depleted, nor that arrythmias resulting from digitalis toxicity will not occur.[18,20,21] Any factor that decreases extracellular potassium or enhances digitalis action can induce arrythmias. Such factors include succinylcholine,[22] catecholamine stimulation, calcium administration, alkalosis,[18] bypass perfusion with dilute solutions,[12] blood volume expansion in hypovolemic patients with potassium deficient solutions, and acute potassium urinary loss.[8,21]

Treatment consists of the administration of intravenous potassium under electrocardiographic control, and removal of the offending agent or technique.

Psychotropic Drugs

I. Phenothiazines

Chlorpromazine and related phenothiazines are generally employed in two situations: 1) treatment of psychiatric disorders and 2) treatment of nausea and vomiting.[23] They possess antiadrenergic, anticholinergic, antihistaminic and antiserotonin activities. They depress endocrine function, interfere with temperature regulation and, generally, depress the central nervous system.[24] In anesthetic practice, these drugs have been used for premedication, to facilitate the induction of hypothermia, and to "spare" the use of barbiturates and narcotics.[23,25]

The effects of chlorpromazine on adrenergic mechanisms are of primary importance to the anesthesiologist. At low dosage, chlorpromazine inhibits uptake of norepinephrine into sympathetic nerve endings and produces primary alpha-adrenergic blockade. With increasing doses, alpha blockade predominates. In the animal central nervous system, chlorpromazine inhibits both the disappearance of radioactive norepinephrine previously taken up into brain, and the electrically induced release of norepinephrine from brain slices.[23] Depression of vasomotor and respiratory centers occurs following injection of the drug intracisternally, intraventricularly or into the vertebral artery.[26] Schmidt suggested that alterations of transmitter physiology, and interactions between chlorpromazine and anesthetic drugs might best be explained by effects on membrane permeability.[23,17]

Hypotension during anesthesia can occur in patients following acute or chronic administration of chlorpromazine, especially if there is pre-existing coronary artery or hypertensive cardiovascular disease.[26] Direct acting sympathomimetic amines provide effective treatment but dosage may have to be increased to overcome the existing alpha-adrenergic blockade.[23] Norepinephrine is more effective than phenylephrine or methoxamine in terms of both dose-response and expected duration of action.[29] Epinephrine has decreased effectiveness against a number of phenothiazines, and reversal of action with increased hypotension occurs in combination with chlorpromazine.[26,28] This is explained by the hypothesis that chlorpromazine has alpha-adrenergic blocking effects which permit unopposed beta-adrenergic effects of epinephrine.[29] Treatment of epinephrine reversal with propranalol has been suggested,[26] but combined alpha and beta blockade may aggrivate hypotension and complicate therapy. For example: subsequent treatment with an alpha-adrenergic drug such as norepinephrine would increase peripheral resistance, but cause a further decline in cardiac output.

Phenothiazines have additive effects when combined with barbiturates, narcotics and anesthetic agents.[24] Dosage schedules must be decreased to avoid excessive depression. The extrapyramidal side effects seen with phenothiazines can become evident during anesthesia as lack of muscle relaxation when usual doses of relaxants are used.[23]

Blunting and widening of the T wave consistently occurs in patients taking Thioridizine (Mellaril) when the daily dose exceeds 300-600 mg., but disappear promptly when the drug is discontinued.[30] Ventricular arrythmias and sudden death were reported in three patients taking doses exceeding 3000 mg of Thioridizine daily. At autopsy, two or these patients showed fragmentation of myocardial muscle and connective tissue deposition.[31] Sudden death has been reported in patients taking chlorpromazine, with acute arrythmia as the implied cause of death. In 12 patients treated with phenothiazines who died suddenly, Richardson found unusual degenerative lesions involving intramyocardial arterioles. Eight of these patients had abnormal electrocardiograms before death.[32]

II. Monoamine Oxidase Inhibitors

The monoamine oxidase (MAO) inhibitors comprise a heterogenous group of drugs which have the ability to block the oxidative deamination of biogenic amines.[23] Structurally, the majority are related to norepinephrine, and are used to treat psychological depression, hyptertension and angina pectoris.[23,33] Those currently in use include nialamide (Niamid), phenelzine (Nardil), isocarboxazid (Marplan), pargyline (Entonyl) and tranylcypromine (Parnate). These drugs inhibit not only monoamine oxidase, but also a wide variety of other enzymes, including succinic and choline dehydrogenase and diamine oxidase. Inhibition of monoamine oxidase is irreversible, and two to three weeks are required to resynthesize enzyme protein and restore function.[23] MAO inhibitors interfere with the metabolism of drugs degraded by the liver microsomal system by inhibiting oxidative enzymes. Drugs affected include barbiturates, narcotics, acetanilid and cocaine.[34]

Interactions between MAO inhibitors and sympathomimetic amines which act indirectly by releasing norepinephrine from nerve endings (tyramine, metamphetamine, mephentermine and ephedrine) have resulted in hypertensive crisis, characterized by incapacitating headache, tachycardia, palpitation, photophobia, sweating and profound hypertension.[35] The crisis may last for hours unless treated. Death from intracranial hemorrhage[36] and acute heart failure[37] has been reported. Two factors are responsible for the development of the crisis: 1) inhibition of degradation of the administered amine by MAO, and 2) the presence of increased concentrations of norepinephrine in sympathetic nerve terminals.[23]

MAO inhibitors interact with many drugs including anesthetic agents, barbiturates, ethanol, analgesics, diuretics, insulin, anti-hypertensives, anti-Parkinson drugs and other anti-depressants.[24] Interaction with barbiturates has resulted in prolonged sleep time and coma;[38] with meperidine in delerium, apnea, hyperpyrexia, coma and hypertensive crisis;[39] with rauwolfia alkaloids, alpha methyldopa and the tricyclic anti-depressants in hypertensive crisis and delerium,[24] and, profound hypotension in combination with thiazide diuretics.[24]

Not all patients receiving MAO inhibitors and other drugs will have adverse reactions. This has been demonstrated for morphine, meperidine and the tricyclic anti-depressants.[24,40] Nevertheless, the high incidence of reactions make it undesirable to subject patients treated with MAO inhibitors to elective surgery and anesthesia. The drug should be withdrawn at least three weeks preoperatively.[23,24] If emergency surgery is necessary, the use of narcotics, particularly meperidine, and barbiturates should be kept minimal. Local anesthetics may be used, but not in combination with vasopressors. Spinal and peridural anesthesia are relatively contraindicated, since vasopressors are frequently included in the local anesthetic drug to decrease absorption and/or prolong the effect. Inhalation agents which increase the circulating level of catecholamines, such as diethyl ether and cyclopropane, should be avoided. Treatment of hypotension with indirect acting vasopressors such as mephentermine is specifically contraindicated. Norepinephrine, in drip form and reduced dosage, has been used with success.[41] Ultra-short acting barbiturates and muscle relaxants have been well tolerated.[35]

In hypertensive crisis, phentolamine (Regitine) effectively reduces blood pressure and relieves symptoms.[23,24] Ventricular arrythmias from beta-adrenergic stimulation have been effectively treated with propranalol. Steroids and chlorpromazine have been used to treat hypertension, hyper-excitability and hyperpyrexia resulting from the combination of meperidine and MAO inhibitors, and steroids have proven useful in the treatment of refractory hypotension.[35]

III. The Tricyclic Anti-Depressants

These drugs are structurally and pharmacologically similar to the phenothiazines, although their anti-depressant actions are unique. Representative drugs include imipramine (Tofranil), desipramine (Pertofrane) and amitripyline (Elavil). They interfere centrally and peripherally with uptake of norepinephrine by sympathetic nerve endings, and in therapeutic doses increase pulse rate and blood pressure. The effect of direct acting vasopressors is enhanced, but indirect acting amines may have reduced effect because they cannot enter the neuron to induce release of norepinephrine.[23,24,42] In animals, large doses have produced hypotension, bradycardia, decreased peripheral blood flow and decreased myocardial contractile force.[26] Orthostatic hypotension, tachycardia, coronary thrombosis, congestive heart failure and pulmonary emboli have been reported in elderly patients with preexisting cardiovascular disease.[26,42] Serious arrythmias on a direct basis have been reported only in cases of acute poisoning.[26,43]

Interactions with other drugs occur, but their frequency and severity are much less than those produced by the MAO inhibitors. Imipramine reverses the sedative effects and mental depression sometimes seen with reserpine, as well as the peripheral antonomic effects of both reserpine and guanethidine.[24,26,44] The reserpine induced depletion of brain and peripheral catecholamines is not affected.[26,44] Imipramine, in moderate dosage, also potentiates the centrally mediated stimulant properties of the amphetamines and methylphenidate (Ritalin), while with large doses there may be blocking. The potentiation is thought to result from a further release of norepinephrine.[44] The central depressant effects of barbiturates and alcohol are enhanced, especially in patients taking large doses of the anti-depressants.[24] In animals, both depression and enhancement (with long term administration) of liver microsomal enzyme activity has been observed.[34]

Irreversible enzyme inhibition and tissue accumulation do not occur with administration of the anti-depressants.[23] If it is felt necessary to withdraw these drugs preoperatively, three or four days is sufficient time. Serious interactions with anesthetic agents have not been observed.

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ANESTHESIA

By 1863 a total of 123 deaths were attributed directly to chloroform in Great Britain alone, and the Royal Medical College, urged on by *The Lancet* and other medical publications, appointed a committee to investigate the subject. This committee, which consulted with two of the leading anesthetics in England, issued a long report in 1864, conceding that chloroform was potentially dangerous and recommending that a search be made for a safer substitute. "Ether," the committee noted, "to a certain extent, fulfills these conditions, but its odour is disagreeable, it is slow in its operation, and gives rise to greater excitement than chloroform." For these reasons, the committee concluded, its use was impractical. Within a few years a gradual improvement in inhalation devices simplified the administration of ether, and it, along with nitrous oxide, gained favor in England, where professional anesthetists were expected to give the patient and doctor some choice in the matter of anesthetic agents. John Snow's example helped to establish in Great Britain the concept that anesthesiology should be a field of its own. This fortunate state of affairs meant that although chloroform remained the prime anesthetic agent in nineteenth-century Great Britain, the creation of a group of relatively skilled anesthesiologists helped keep the number of deaths to a minimum.

In the United States in these years anesthetization was essentially a slapdash procedure. Usually chloroform was simply poured on a handkerchief or piece of cloth held over the face of the patient. A Texas physician reported in 1876 that, during a difficult labor lasting 30 hours, he had used 17 ounces of chloroform, but he admitted that the imperfect administration of the anesthetic led to much wastage—a fact which may well account for the mother's survival! Ordinarily the anesthetic was given by the attending physicians, most of whom were convinced that chloroform was absolutely safe and could be sloshed on a towel or cloth with more or less impunity. Fortunately, as the 19th century drew to a close, inhalation devices were adopted in most of the better hospitals, but the average general practitioner still continued to use sponges, towels, handkerchiefs, or whatever else was available.—Duffy, J.: Anglo-American Reaction to Obstetrical Anesthesia, *Bull. Hist. Med.* 38:32-44 (Jan.-Feb.) 1964.

Professional Liability of Anesthesiologist

Frank A. Manthey, M.D. and William R. Murphy*

Among the medical specialities highly exposed to malpractice claims is the practice of anesthesiology. Thus, a study of 700 professional liability claims in California published in 1957 indicated that anesthesiologists ranked second only to surgeons in the total number of such claims studied[1]. In the experience throughout the country of the Insurance Rating Board, a rating bureau of insurance carriers writing medical malpractice coverage, anesthesiology ranks along with various other high-risk surgical specialties such as neurosurgery, orthopedic surgery and plastic surgery as among the most hazardous medical specialties from the viewpoint of professional liability.

The legal principles applicable to malpractice claims against anesthesiologists may be stated in the same general terms as are applicable to other fields of medical practice. In its barest form, the fundamental proof which a plaintiff must establish in such a case is that the defendant physician failed to exercise that degree of care, skill or diligence ordinarily had and exercised by physicians engaged in the same line of practice in the general neighborhood where the treatment complained of was administered. More specifically, anesthesiologists are judged by the standards of care, skill and diligence ordinarily had and exercised by other anesthesiologists in the same general area. Absent an express promise, they are not guarantors of a favorable result, nor are they liable for bona fide errors in judgment where they exercise the requisite degree of care, skill and diligence as set forth above.

Although this statement of the basic doctrine is relatively simple, its application to a particular case becomes more difficult. In consonance with the basic rule, the Connecticut courts have stated that, if a defendant *general practioner's* treatment is properly to be tested by the above standard, it necessarily follows that such a defendant is not required to use a degree of care commensurate with that exercised by those classified as experts in a specialty. Thus, the Connecticut Supreme Court has stated that "(a) country general practioner should not be expected to use the high degree of skill possessed by eminent physicians living in large cities and specializing in various branches of medicine[2]". Even within a specialty, the law does not require of a physician the utmost degree of care or skill known or obtainable to the profession. But standards of practice in virtually all specialty fields are now heavily influenced by national specialty boards. What impact do such Boards have, therefore, on the legal standards applicable in a field such as anesthesiology where a relatively high percentage of the specialists are exposed to board-certification standards on a national level designed specifically for the purpose of raising the national standards of practice within the specialty? Most general hospitals in Connecticut have one or more anesthesiologists practicing in them who are either board-certified or board eligible. And in many, perhaps most, of such hospitals, the individuals so qualified are in positions of responsibility such that they can establish or influence standards for the anesthesia department. Does this mean that, within a specialty such as anesthesia, traditional statements of the "general neighborhood" or "locality" concept give way in actual practice to a more nearly national standard keyed directly to norms established by the American Board of Anesthesiology?

There has been—particularly in certain other jurisdictions—substantial erosion of the locality rule. The Connecticut Supreme Court, which has generally followed a somewhat more traditional (and, we believe, fairer) approach to medical malpractice claims than has been pursued in certain other states, continues to adhere to the locality standard. Even in Connecticut, however, there has been some tendency in recent years to permit evidence of the applicable standard of practice to be established other than by the direct testimony of physicians practicing in Connecticut. Thus, the Connecticut Supreme Court has stated that the mere fact that a physician has not practiced in the immediate neighborhood in which the alleged malpractice has occurred does not necessarily disqualify him from testifying as to the standards of practice in that locality. The Court has indicated that

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"(t)he crucial question is whether he knows what these standards are[3]". Although this rule is not, and should not be, interpreted so broadly as to permit testimony as to Connecticut practice from witnesses lacking an adequate basis for knowledge of such practice, it would appear that it is broad enough to permit testimony on the basis of national standards known to the witness to apply to all specialists in anesthesiology, including those in Connecticut.

We believe that certain national standards of care, skill and diligence have been established concerning some fundamental aspects of the practice of anesthesiology. Departure from these basic standards is likely to render the anesthesiologist liable in a malpractice suit where injury results from such departure. Use today of the once-accepted practice of sterilizing ampules used for spinal anesthesia by soaking them in alcohol, for example, is no longer acceptable and would seem to fall into this category. Similarly, the performance of general anesthesia without having equipment for the suctioning of the patient reasonably available would fall below such standards. This does not mean, however, that there has been a complete abrogation of the locality rule in favor of national standards of practice. Certain standards of care may, in fact, vary from area to area. In some areas, for example, a tonsillectomy under general anesthesia without use of an endotracheal tube would not be accepted practice, whereas in other areas use of an endotracheal tube is not required for the procedure. As to such matters, we believe that expert testimony from a physician having experience in a particular locality will still be required.

What is perhaps most important from the viewpoint of preparing an anesthesia malpractice case, however, is the need to distinguish true standards of care from mere differences in technique. The question of whether or not an examination should be made of the patient's mouth before certain procedures, for example, would involve a standard of care. On the other hand, the type of airway or type of pre-operative medication which the anesthesiologist might select for the procedure would, in many instances, simply involve questions of variations of technique unrelated to standards of care. Each technique may have its own advantages and disadvantages. Often, such variations in technique simply reflect differences in approach as taught in various medical centers. Anesthesiologists have a high degree of mobility. As they move into new areas, they will naturally take with them the techniques which they have acquired at the various centers at which they have trained or practiced. Often one technique has no clear advantage over others—the selection of one over others ultimately amounting simply to a question of individual preference.

Where the technique of one anesthesiologist varies from that used by others in the same general neighborhood, there is always the risk that a court or jury, attempting to apply the appropriate general legal principles to the specific fact situation before it, will find that the difference in technique amounts to a departure from a proper standard of care. There is no sure way of avoiding the possibility that such a conclusion will be drawn. With respect to this problem, however, increasing recognition of essentially national standards of practice may be of benefit to the anesthesiologist. The law recognizes that where there is more than one recognized school of medical practice, a defendant physician is to be judged by the standards applicable to the school to which he belongs[4].

We believe that, where differences in technique are involved, development at trial of an adequate factual record which demonstrates that the technique in issue is one which is well-recognized and accepted by a substantial number of specialists in anesthesiology throughout the country will help to protect an anesthesiologist against an unwarranted finding of malpractice. Such evidence can be presented most clearly and persuasively if anesthesiologists practicing in the general area where the claim arises are genuinely familiar with the technique in question and are prepared to acknowledge, where they hold such beliefs, that use of such technique does not mean that the defendant anesthesiologist has departed from the standards of care, skill and diligence ordinarily had and exercised by such specialists in the locality. Participation in the activities of the American Board of Anesthesiology, attendance at professional conferences and attention to pertinent professional literature are obviously of tremendous benefit in providing the necessary foundation for such evidence.

A further question of significance in considering the professional liability of anesthesiologists is the question of the patient's consent. Justice Cardozo, while a judge on the New York Court of Appeals, stated the applicable basic principle in an oft-quoted opinion as follows:

> "Every human being of adult years and sound mind has a right to determine what shall be done with his own body; and a surgeon who performs

> an operation without his patient's consent commits an assault for which he is liable in damages. This is true except in cases of emergency where the patient is unconscious and where it is necessary to operate before consent can be obtained[5]".

In light of this basic requirement for consent, an anesthesiologist who administers anesthesia without the consent of a patient, may be found liable for an assault on the patient. Proof of such assault entitles the plaintiff to a verdict for at least nominal damages and to such special damages in addition as the plaintiff has alleged and proved to have proximately resulted from the assault[6].

Perhaps the greatest risk to an anesthesiologist likely to arise from an "assault" having its genesis in failure to obtain the patient's consent to anesthesia, is the possibility that complications directly traceable to the anesthesia may arise. It is not necessary in order to prove such an assault that the plaintiff establish that the procedure was in any way unskillfully performed. Consequently, to the extent that complications may be found to be directly attributable to the anesthesia, there is a risk in such cases that the anesthesiologist may be held liable in damages for such complications.

Clearly, express written consent, freely given by an adult of sound mind (including the parent or guardian of a minor child) in the presence of an independent witness, is desirable in all cases where possible. It is not absolutely essential, however, that consent be written or even express. Consent can be implied from conduct or circumstances. If an adult patient in control of his senses silently offers his arm for placement of an intravenous infusion after being informed by a physician that this is what he proposes to give, for example, consent will ordinarily be inferred. The same is true where a parent, having been informed of a physician's proposed course of treatment, stands silently by and offers no objection as the physician prepares for and undertakes such treatment. Where objection is offered or questions are raised, however, the physician should not proceed with the contemplated action until it is clear that the necessary consent has been obtained. In dealing with adults, physicians should remember that it is the individual himself—not the spouse or the child of an elderly parent or another relative—who must give consent. Only a court-appointed conservator of the person has any legal authority to give consent on behalf of an adult who is not himself legally competent. Although it may be desirable from a practical viewpoint to obtain the written consent of a close relative in addition to the consent of the patient himself where the patient is aged and infirm, the necessity for the patient's personal consent should not be disregarded.

A related and often-discussed issue which has arisen, particularly with reference to various types of surgery and high-risk procedures, is the question of "informed consent". Briefly, this concept deals with the extent to which there is an obligation upon the physician to make known to the patient sufficient facts as to risks involved in the proposed treatment so as to form the basis for an intelligent consent on the patient's part.

There appear to be few reported cases throughout the country in which claims based upon informed consent have been made against anesthesiologists. In general, the reported rulings on this question have been favorable to the anesthesiologists. In one case in which a patient claimed that her vocal cords were damaged during intubation, for example, the court concluded that, absent inquiry, it would not be reasonable to require that the patient be informed in advance as to the proposed method of anesthesia (halothane by use of an endothacheal tube) and of all possible risks involved in each step of the operation; and in another, the court concluded that, where a maternity patient had made no inquiry, "there was no duty upon (the defendant) *in this case* to warn (the patient) of *possible* consequences or to obtain her specific consent to a spinal anesthetic". (Emphasis in original opinion[8]). In a 1968 opinion, however, the Texas Supreme Court held that there were issues requiring a factual trial where only the plaintiff's husband had given written consent to anesthesia and the plaintiff contended, in contradiction to certain other evidence, that she had not and would not have consented to a spinal anesthesia[9]. The Supreme Court did not rule upon claims of informed consent, ruled upon adversely to the plaintiff by the intermediate appellate court[10], on the ground that the evidence at trial might prove different from that in the record then before it on defendants' summary judgment motion.

One possible reason for the relatively small number of "informed consent" claims against anesthesiologists in the reported cases is the fact that major complications from anesthesia are relatively infrequent when measured statistically against the number of anesthesias of virtually every type which are performed annually. Spinal anesthesia, for example, which is often regarded by laymen as involving higher risks than various other anesthesias, has been shown to have an excellent record of relative freedom from serious complications[11]. And although it is difficult to draft any definitive rules as to just how much advance disclosure of possible adverse consequences is required to make the patient's consent an "informed" one, it is certainly true that the more remote the possible complication, the less likely it is that a court will impose upon a physician the duty to warn concerning it.

The above comments should not be interpreted to mean, however, that anesthesiologists can afford to ignore completely developing concepts of informed consent. Reported cases, most of which are ones which have reached appellate levels, represent but a relatively small percentage of the total number of malpractice cases decided each year in our courts. Moreover, the same fundamental principles which are being developed with respect to other specialties will be applied to anesthesiologists. It is not within the scope of this article to attempt a full discussion of informed consent[12]. We shall, however, attempt to outline a few fundamental precepts which we feel should guide physicians, including anesthesiologists, in seeing that a patient's consent is truly an informed one.

Because the law concerning informed consent is developed throughout the country on a case by case basis, it is not practical to attempt to set forth a precise check-list to which an anesthesiologist may refer. Obviously, several hours might be needed to explain fully all aspects and dangers, however remote, that could result from a procedure as simple as starting an intravenous infusion, and the anesthetic management of the simplest surgical procedure. Disclosure of this nature is impractical, unnecessary and likely to be harmful to the patient. A reasonable compromise must be drawn. The most important consideration is that the anesthesiologist communicate with the patient honestly. The patient's questions must be answered truthfully in terms which he can understand. Also, the greater the degree of probability there is that certain sequelae will result, the greater is the obligation of the anesthesiologist to disclose such risks. To the extent that certain permanent sequelae are likely to result to a patient from a given procedure, such as the high incidence of male impotence after abdominal perineal resection, for example, the patient should be made fully aware of such consequences so that he may balance this detriment against the anticipated benefits of the procedure. Moreover, even where the patient does not inquire about risks affirmatively, we believe that the anesthesiologist should inform him of potentially adverse consequences which there is a reasonable likelihood may arise.

Perhaps the greatest risk in anesthesia arises as a result of a generally poor physical condition of the patient. Where such risks are involved, we believe that it would be highly desirable not only that both the physician having general responsibility for the patient and the anesthesiologist should each see the patient to discuss the anticipated treatment with him but also that both physicians should confer directly with each other concerning his condition. This has the advantage from the anesthesiologist's viewpoint of making possible an exchange of opinions with a physician having a more intimate knowledge of the patient and of his medical history. There will be instances in which a full disclosure of risks cannot be made to the patient without the likelihood that the disclosure itself will have a materially adverse effect on the patient. Under such circumstances, there are clear evidential advantages from a medico-legal viewpoint arising from the fact that such a decision has had the concurrence of both physicians.

Where it appears that it would be detrimental to the patient's welfare to advise him fully as to the risks he faces, it is desirable from a practical viewpoint that information as to the nature of such risks be communicated to the patient's relative or relatives most directly concerned. Apart from such communication made to the parent or guardian of a minor child or to the court-appointed conservator of an incompetent, such communication probably does little to relieve the physician of whatever obligation of disclosure to the patient himself may be imposed by law under all of the circumstances of the case. Most lay people realize, however, the difficult problems faced by physicians in the treatment of high-risk patients. And numerous studies have demonstrated that much malpractice litigation arises out of a breakdown in communication between physicians and their patients or the patients' relatives. Communication to the patient's family will therefore tend to reduce the likelihood that a malpractice claim will be instituted as a result of unfavorable results of treatment. Moreover, where suit does result, such action by the physician can be of tremendous psychological value in persuading the judge or jury deciding the case that the physician has conducted himself reasonably under all of the circumstances.

It is clearly important in all aspects of medical practice that physicians make adequate records of pertinent observations, discussions, treatments and medications ordered and used. Such records are not only required for good medical practice but also are of value in the protection of the physician himself against unmeritorius malpractice claims. We believe that the fact that the proposed anesthesia has been discussed with and explained to the patient (or the patient's relatives, where appropriate) is a relevant fact which should be recorded in the hospital record.

Although any discussion of medical malpractice must of necessity focus to some extent upon the consequences of potential derelictions on the part of physicians, the legal principles by which the conduct of physicians is tested are not unduly restrictive. Rather, at least as applied generally in Connecticut, those principles are founded upon and in consonance with good medical practice. By simply following such practice and by communicating his decisions and the reasons for them to the patient and the patient's family in terms which they can understand, the anesthesiologist will do much to protect himself against unwarranted claims.

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12. For more complete discussion, see Louisell and Williams, *Medical Malpractice,* 1969 ed., Chapt. XXII.

One evening in the late eighteenth century an Italian woman stood in her kitchen watching the frog's legs which she was preparing for the evening meal. "Look at those muscles moving . . . . they always seem to come alive when I hang them on a copper wire.

Her husband Luigi Galvani looked . . . . The cut end of the frog's nerve was in contact with the copper wire and electric current produced by the contact was passing along the nerve to the muscle. As a result the muscle was twitching and contracting.

He had discovered the key to electricity and to nerve conduction and to muscle action. Here was the basis of all animal movement reflex and voluntary in frog and man.—*Wilder Penfield in The Second Career. "The Physiological Basis of the Mind—Familiar Medical Quotations by Maurice B. Strauss.*

Respiratory Intensive Care

James I. Gilman, M.D.

Life threatening conditions amenable to surgery appear in all body systems. Surgeons are no longer reluctant to operate on severely ill patients exhibiting multiple complex problems. Age barriers to surgery no longer exist; the newborn and the nonagenarian enter the operating room for similar procedures. Although the scope of problems of management before, during, and particularly after surgery has increased in advanced states of disease or massive injury, the patient usually survives operation.

The anesthesiologist provides artifical ventilation and respiratory care for the patient during operation. Respiratory management of the post-operative patient, in the surgical intensive care unit will be discussed in this paper.

Evalution of Ventilation

Both qualitative and quantitative means exist to judge respiratory insufficiency. Qualitatively, ventilation can be assessed by the appearance of the patient; whether he is quiet, restless or struggling to breathe. Retraction of soft tissues at the suprasternal notch, intercostal spaces, or abdominal wall indicates upper airway obstruction; the use of accessory respiratory muscles points out increased work of respiration. Nasal flaring occurs with hypoxia, hypercarbia and increased respiratory effort. A chest fixed in inspiratory position suggests chronic or acute air trapping, or emphysematous lungs. Paradoxical chest motion suggests a flail chest, or upper airway obstruction in a patient with a very compliant chest wall. When increased resistance to airflow exists, as with broncho-construction, compensation is by long slow respirations. When increased elastic or tissue resistance exists, as with inflammation or fibrosis, compensation is by shallow rapid respirations[1]. Gross cyanosis appears when oxygen saturation of the hemoglobin is below 75%, but variations in light intensity and the color of surroundings, have an effect on recognition of cyanosis.

Quantitative methods for evaluation of respiration include direct measurement of pulmonary function. The Wright^R respirometer and a watch measures tidal volume, minute volume, vital capacity, and timed vital capacity. A simple recording spirometer shows inspiratory and expiratory reserve, and the rate of forced expiration.

Patients with a vital capacity less than 2½-3 times predicted tidal volume usually are unable to cough up their secretions sponsaneously.

Blood Gas Studies

Arterial blood gas and pH determinations provide the most accurate method of evaluation of the efforts to breathe, and are the best indication of respiratory sufficiency, or the need for artificially assisted or controlled ventilation.

Arterial pH has a normal range from 7.35 to 7.45. A fall in pH may result from metabolic effects such as ketoacidosis or lacticacidosis following tissue hypoxia, hypoperfusion or starvation. Since acid urine excretion is a slow process, the body responds to sudden metabolic acidosis with hyperventilation, eleminating H^+ by exhaling CO_2 $(H^+ + HCO_3 - \rightarrow H_2CO_3 \rightarrow H_2O + CO_2)$ because metabolic acids are not volatile. The result is lowered PCO_2 and lowered HCO_3^-, or total CO_2. A fall in pH also results from respiratory insufficiency with rising $PaCO_2$, called respiratory acidosis. The pH and $PaCO_2$ are related as shown by the Henderson-Hasselbach equation: $pH = 6.1 + \log \frac{HCO_3}{H_2CO_3}$, where (H_2CO_3) equals 0.03 x $PaCO_2$. An acute, uncompensated rise in $PaCO_2$ of 10 torr will lower the pH approximately 0.04 units. Respiratory acidosis with pH below 7.2 and $PaCO_2$ above 60 torr both indicate the need for artificial respiratory support.

CO_2 is transported in solution, as HCO_3^-, in combination with blood buffers, primarily hemoglobin. The PCO_2 follows alveolar ventilation in a linear fashion, for example, doubling ventilation will halve the PCO_2. Normally the body responds to increased $PaCO_2$ by increasing ventilation, primarily increasing rate, then increasing depth. Resting tidal volume may be estimated at 3 ml per pound of body weight. The normal relation

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of dead space to tidal volume, called the V_D/V_T ratio, is 30% or less. When the ratio exceeds this level, respirations increase to compensate for increased CO_2. The body can compensate for a larger dead space by increasing minute and alveolar ventilation, but above 50% or 60%, the ventilatory volume required usually surpasses the respiratory capacity, fatigue occurs, and CO_2 rises to anesthetic levels (80 to 100 torr). At the amount of ventilation required, the work of breathing rises from the normal of 1.2% of total oxygen consumption to 15-20%. We have treated patients who have required 25 to 30 liters minute ventilation to maintain a normal $PaCO_2$.

Artificial ventilation removes the work of respiration. If ventilatory requirements are greater than normal, dead space reduction with an endotracheal tube or tracheostomy, and the use of a ventilator satisfies respiratory needs at a level below that which the patient himself was forced to maintain alone. While pH and PCO_2 can be evaluated from venous blood samples, the arterial PO_2 is the best measure of oxygenation. Simultaneously measured inspired oxygen concentration allows calculation of venous admixture or intra-pulmonary shunt. When the inspired oxygen concentration is 21% (room air), the P_aO_2 should be approximately 95 torr. Normally, the alveolar PO_2 (P_AO_2) breathing room air, is approximately 100 Torr, producing an alveolar-arterial (A-a) gradient of 5 Torr. A fall in P_aO_2, or increase of the (A-a) O_2 gradient, denotes increased venous admixture.

The normal hemoglobin-oxygen dissociation curve describes the saturation for any given PO_2 with a sigmoid curve. At a PO_2 of 90 torr, the saturation is 96%. The upper arm of the curve is relatively flat, and a fall in PO_2 to 60 torr still maintains 90% saturation. However, below 60 torr the curve steepens, and at 30 torr, the saturation is down to 50%. The dissociation is affected by blood pH, with the curve shifting to the right, producing a lower saturation at a given oxygen tension. Aortic and carotid chemoreceptors respond to a falling P_aO_2 rather than saturation, causing compensatory increase of ventilation. If the fall has been gradual, there maybe little response until the P_aO_2 falls below 60 torr.

When the P_aO_2 falls below 75 torr, application of corrective measures is indicated. Although oxygen enrichment provides immediate improvement, it rarely provides long term benefit. The most common cause of hypoxia is scattered atelectasis in areas too small to be seen roentographically. Inadequate hyperexpansion, or sighing, may lead to progressive atelectasis, and, pain, respiratory depression, or mechanical restriction may extend this process. Retained secretions may block small bronchioles and produce maldistribution of gases or alveolar collapse. Because of the structure of alveoli and lining surfactant, ventilatory pressure required to re-expand a collapsed alveolus is greater than that required to keep it open. Coughing and sighing normally provide the force required to expand small degrees of atelectasis, but in widespread collapse, extra work is necessary to reexpand alveoli. Progressive atelectasis lowers compliance, and increases the work of respiration. If the patient is conscious and cooperative, the use of a patient-cycled, pressure limited ventilator supplies the extrapulmonary expansion needed to prevent atelectasis. The uncooperative or unconscious patient requires more vigorous therapy, with an endotracheal tube or tracheotomy. When pulmonary function studies (e.g. tidal volume, minute volume, and arterial gases) indicate the presence of respiratory failure, and simple means do not provide adequate correction, more extensive measures must be instituted.

In prolonged intensive care, an indwelling arterial catheter offers advantages of constant monitoring of the blood pressure, and repeated blood gas sampling. The radial artery is the vessel of choice, after assuring the patency of the ulnar artery. Periodic flushing with dilute heparin solution maintains the patency of the vessel and cannula.

Endotracheal Tubes and Airway Management

Oral or nasal endotracheal intubation provides a patent airway for ventilation, a pathway for tracheal suctioning, and a method of preventing aspiration of gastric contents. The nasal route is the better choice when intubation must be maintained for several days because of ease of fixation and less discomfort, however increased airway resistence and restriction of the lumen are disadvantages. Except in children, nasal or oral tubes should have inflatable cuffs to insure tight seal. One child who required prolonged artificial ventilation with a nastotracheal tube was able to eat ice cream and other soft foods and liquids while intubated. When prolonged artificial ventilation is anticipated, tracheostomy simplifies nursing and ventilator care. The Portex^R tracheostomy tube has a 15 mm male-male connector for attachment to the ventilator, the self-filling ventilating bag, or an anesthesia machine.

Precise airway management and tracheobronchial toilet are the sine qua non of an intensive care unit. The depressed patient with an artificial airway is unable to clear his own secretions by coughing. Respiratory intensive care procedures maintain an unobstructed and uncontaminated airway. Hourly suctioning is usually necessary. Hyperexpansion of the lungs prior to suctioning loosens secretions, and reduces the risk of hypoxia or hypercarbia. Arrythmias and cardiac arrest can occur during prolonged suctioning. Sterile saline, 1-5 ml. instilled in the endotracheal tube before suctioning will facilitate the removal of tenaceous secretions. Suctioning technique should include the use of sterile gloves, and sterile disposable suction catheters, which should be discarded immediately. Containers of sterile saline used to clear catheters during suctioning should be discarded after 4 hours. Strict precautions are not needed for mouth or pharyngeal suctioning, since these areas are not sterile, but pharyngeal suction catheters should not be used for tracheal suctioning.

Judicious intravenous use of small individualized doses of narcotics (meperidine 5 to 10 mg; morphine 1 or 2 mg) will reduce the patient's respiratory drive, and aid adjustment to the ventilator. Deterioration despite adequate ventilation and sedation may necessitate use of paralyzing agents. Intravenous d-tubocurare in small doses (3 to 6 mg every 30 to 60 minutes) will provide relaxation necessary for respiratory control. Sedation with barbiturates and/or tranquilizers may reduce psychic trauma and permit sleep between periods of stimulation.

Ventilators

Ventilators are pressure limited or volume limited. The Bird^R respirator is a typical pressure-limited ventilator. Inspiration may be initiated automatically or by the patient. Inspiratory flow rate is adjustable, and pre-set pressure limits tidal volume. Precise control of oxygen concentration requires an extra source of compressed air. High airway resistance, low compliance, and large volume requirements often make this ventilator inadequate.

The Emerson Postoperative Ventilator^R supplies a pre-set volume of gas, regardless of airway resistance or compliance, with simple control of oxygen concentration. This ventilator administers a periodic hyperexpansion as well as heated, humidified gas, but it does not allow patient cycling.

The Bennett MAI and Ohio 560 ventilators are more versatile volume ventilators providing direct selection of oxygen concentration, provision for patient cycling, better control of inspiratory and expiratory phases, and more precise automatic cycling.

Ventilation

Regardless of the specific ventilator selected, a large tidal volume at a slow rate provides good alveolar expansion and gas distribution, maintaining optimum minute ventilation while decreasing intrapulmonary shunting. Tidal volume set at 2 to 3 times the predicted resting volume will reduce atelectasis. The minute ventilation (tidal volume x rate) required can be determined by the following $PaCO_2$ serially. A respiratory rate as slow as 8 per minute, combined with a tidal volume of 1000 to 1500 milliliters, will provide adequate ventilation with reasonable patient comfort. Occasionally the $PaCO_2$ falls to 20 torr or lower with the large tidal volumes required. When this occurs extra dead space is provided with additional flexible connector tubing between the endotracheal tube and ventilator. An intermittant sigh reduces the need for continuously large tidal volumes if low compliance demands peak pressure in excess of 35 cm H_2O. High mean airway pressure and large tidal volume are contraindicated when emphysema, pneumothorax, or hypovolemia is present.

Oxygen Toxicity

Prolonged exposure to high concentrations of oxygen leads to pulmonary oxygen toxicity. The signs are falling compliance and falling P_aO_2 despite an elevated inspired oxygen concentration. In the early stages, increased minute ventilation lowers $PaCO_2$, but does not raise the PaO_2 significantly. Radiographically, there may be no evidence of atelectasis. Progression of the processs further lowers the compliance, increasing the A-aO_2 gradient, and finally raising $PaCO_2$ despite increased minute ventilation. An x-ray may reveal diffuse widespread haziness or "ground-glass" appearance.

Pathologically, the process begins as edema or thickening of the alveolar wall and septa, and progresses to fibroblastic cellular infiltration of the interstitial tissues, and deposition of an alveolar hyaline membrane, pulmonary atelectasis, and, terminally, consolidation of the lobes[2]. If the patient survives, healing produces extensive fibrosis. Some children appear free of damage several years after the injury, while others have become respiratory cripples.

Etiologically, oxygen toxicity is presumed to cause changes in cellular metabolism initiated by increased oxygen tension, with disruption of enzyme systems. Correlation between the inspired concentration, length of exposure to increased oxygen tension and the degree of injury has been shown, but the degree of injury does not appear related to mechanical ventilation[3] Toxic changes rarely occur with oxygen concentration below 40%.

Recently animal experiments have shown that pulmonary oxygen toxicity can occur from increased inspired oxygen concentration, despite an anatomical right to left shunt, with lowered peripheral P_aO_2 and cyanosis. In other words, peripheral arterial hemoglobin desaturation does not protect against oxygen poisoning[4]. No specific treatment is known. The best prevention is maintainance of inspired oxygen concentration as close to 21% as possible, consistent with a P_aO_2 above 60 torr.

Weaning and Extubation

Extubation follows the procedure of weaning from controlled ventilation by short periods of unassisted ventilation which allow return of respiratory strength. Humidified 40% oxygen supplied to the endotracheal tube or tracheotomy prevents hypoxia or inspisation of secretions during the process. When the patient can maintain normal blood gasses for 1 to 2 hours duration, the tube may be removed. IPPB by mask or mouth piece assists the patient in spontaneous coughing and expectoration.

Summary

Intensive respiratory care has become a specialty unto itself. This discussion has enumerated the steps in the diagnosis and treatment of respiratory insufficiency. The importance of meticulous detail while avoiding the iatrogenic oxygen toxicity has been emphasized.

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THE IDEAL PHYSICIAN

He is first and foremost humane
He is constantly observant
He uses a systematic approach
He knows and understands basic principles
He uses reason in all his actions
He is aware of the limitation of his own knowledge
and of knowledge in general
He respects the information that comes from all
He is a perpetual student—Wm. L. Morgan, Jr.
and George L. Engel. *Introduction to the Patient,* Chapter One in the *Clinical Approach to the Patient.* Philadelphia,
W. B. Saunders, 1969, pp. 14-15.

Muscle Relaxants and Some Problems With Their Use

B. Barry Greenhouse, M.D.

An increasing tendency exists in some departments of Anesthesiology to use light general anesthesia supplemented by muscle relaxants to provide adequate surgical conditions. Rational use of muscle relaxants requires: (1) knowledge of the physiology of the myoneural junction; (2) understanding of the pharmacology of the relaxants and their antagonists; (3) a method for determining the magnitude and duration of action of the muscle relaxants in a given patient; and (4) familiarity with the side effects and complications of the different relaxants.

Studies with the electron microscope have revealed that the anatomy of the myoneural junction consists of the presynaptic neural area which is separated from the fluted postsynaptic membrane by the synaptic gap[1]. The effect of drugs on neuromuscular transmission causes alteration of the normal chemistry of synaptic activity. Acetylcholine is the transmitter substance, which is synthesized and stored bound to protein in presynaptic vesicles until liberated by a bioelectrical event, the nerve impulse[2]. Theoretically, quanta of the transmitter substance are released into the synaptic gap during vesicle rupture. The liberated ester diffuses across the gap to react with the cholinergic receptor. The union of acetylcholine with the cholinergic receptor induces alteration in the chemical conformation of the receptor. This alteration also effects a change in the conductance of sodium and potassium ions and triggers the fall in the postsynaptic membrane potential generating a self-propogating action potential[3].

The relationship between acetylcholine and the postsynaptic membrane receptor is a state of dynamic equilibrium. The activity of acetylcholine is terminated by reducing its concentration in the receptor area. Acetylcholinesterase hydrolyzes the free ester rapidly. As acetylcholine concentration falls, the receptor mechanism is reconstituted as sodium and potassium ion movements re-establish postsynaptic membrane potential[4].

The muscle relaxant drugs have been divided into depolarizing agents and non-depolarizing agents. The former include succinylcholine, decamethonium, and imbretil, and, the latter d-tubocurarine, dimethyl d-tubocurarine and gallamine.

The nature of the block produced can be determined by measuring the response of muscle-to-motor nerve stimulation[5]. The "Blockaid Monitor" marketed by Burroughs Welcome Co., and the Churchill-Davidson modification of it are examples of monitoring equipment which may be used for this purpose. The monitor produces a single twitch every 4 seconds of 25-30 millivolt magnitude. The tetantic stimulus is 25-30 millivolts per second. The electrodes are usually placed along the course of the ulnar nerve at the wrist or elbow[6]. Clinically, the monitor will determine: (1) the magnitude of the neuromuscular block, (2) the nature of the block, i.e. depolarzing or non-depolarizing, (3) the need for antagonist therapy.

When non-depolarizing relaxants are used, poorly-sustained tetanus, post-tetantic facilitation and fade of successive single responses are observed. Depolarizing muscle relaxants are characterized by well-sustained tetanus, absence of post-tetanic facilitation and no-fade of response to successive single twitches.

Succinylcholine is characterized by a brief duration of action[7]. Rapid hydrolysis of the succinylcholine by plasma cholinesterase, produced in the liver, accounts for this. Prolonged response to sucsinylcholine can be seen (1) in patients with atypical plasma—or pseudocholinesterase; (2) with the development of dual block; and/or (3) after continuous infusion of 500 mgs or more of succinylcholine. Bourne, et al. found that prolonged apnea following the use of succinylcholine was occasionally associated with low plasma cholinesterase activity[8]. Forbat, et al. reported that the low enzymatic activity might be inherited after finding low serum cholinesterase levels in two brothers[9]. Lehman and Ryan suggested that a recessive gene is

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responsible for low serum cholinesterase activity[10]. Kalow and Genest developed a simple test for differentiating the enzymes. This test involves the determination of the degree of inhibition of plasma cholinesterase activity by the local anesthetic, dibucaine. The percentage inhibition obtained is called the dibucaine number and has a value of about 20 for persons with atypical enzyme, and about 80 for normal patients. A third group of individuals have dibucaine numbers of about 60 indicating the synthesis of both normal and abnormal enzymes in equal amounts. Approximately 97% of the population have a dibucaine number of 80, 3% have a dibucaine number of 60 and 1:2800 have a dibucaine number of 20[11].

The incidence of development of a dual block is related to the duration of depolarization of the myoneural junction. Patients given a single intravenous injection of 4 mgs/Kg of succinylcholine showed prompt recovery with no measurable evidence of a dual block. Patients given a similar dose intramuscularly had a longer duration of depolarization and showed 73% incidence of a dual block[12]. Katz has shown that succinylcholine 3.0 mgs/Kg given by a slow intravenous drip causes 100% incidence of a dual block[13].

Five stages have been described in the development of a dual block

(1) Depolarizing stage—Described previously.

(2) Tachyphylaxis—Repeated doses of succinylcholine result in a diminished response. To reestablish the initial response, it is necessary to increase the dose.

(3) Wedensky inhibition—There is a "fade" response by the muscle to repeated tetanic twitches to the nerve as observed with the monitor. The single twitch response remains unaltered.

(4) Fade and Facilitation—Single twitch response fades and repetitive stimuli and post-tetanic facilitation become evident.

(5) Non-depolarizing Stage—Typical curare-like response is observed.

Stages (4) and (5) can be reversed by an anticholinesterase drug. Foldes showed that the rate of urinary excretion of succinymonocholine was ten times as prolonged as the rate of excretion of succinydicholine. When an excess of 500 mgs of succinyldicholine was given, enough monocholine remained unhydrolyzed to provide a neuromuscular block[14]. Prolonged apnea will result and artificial respiration will be necessary until the monocholine has been hydrolyzed.

Cohen et al. have shown that combined renal and hepatic elimination of d-tubocurarine accounts for over 85% of the injected dose within 24 hours[15]. In the absence of renal function, the liver increases its capacity to transport d-tubocurarine into the bile. A search for metabolites of d-tubocurarine in urine and bile indicated that no metabolites were present in urine, but that approximately 1% of the injected dose appeared in the bile in alternate molecular form. In nephrectomized patients, Churchill-Davidson showed that the duration of action of d-tubocurarine is not unduly prolonged in complete absence of renal excretion, suggesting that the length of paresis is related to dilution and re-distribution rather than to urinary excretion[16].

Pyridostigmin has been found to be superior to edrophonum and equal to neostigmine as an antagonist of d-tubocurarine. Pyridostigmin produced fewer oropharyngeal secretions and decreased heart rate less often than neostigmine[17]. However, pyridostigmin has not yet been approved for intravenous use and neostigmine remains the drug of choice at the present time for curare reversal.

Katz recommends 1 mg of atropine for every 2.5 mgs of neostigmine with the atropine given one minute prior to injection of the neostigmine[18]. Churchill-Davidson recommends the same combination in single intravenous mixture. The mixture is given slowly over a 5 minute period with careful pulse rate monitoring.

The use of muscle relaxants is not without side effects which include: Differences in effect related to age, cardiovascular effects, increases in intraocular pressure, central and autonomic nerve system effects, cardiac arrythmias, generalized myotonia and prolonged respiratory depression.

On the basis of body surface area, newborn and adult patients were given d-tubocurarine, 4 mg/m^2 respectively. The duration of action was evaluated by observing the muscle response to nerve stimulation. Little difference was found between the duration of action of succinylcholine in newborns and adults. Newborns and infants were more sensitive to d-tubocurare than adults[19]. Stead reported that newborns and adults respond differently to muscle relaxants, assessing responses by ventilatory depression and concluded that neonates *require twice* the dose of succinylcholine in mg/Kgs[20]. Churchill-Davidson and Wise using electromyographic techniques, that the newborn was resistant to decamethonium and required two to three times the adult dose. They were unable to confirm Stead's finding regarding the higher sensitivity of the infant to d-tubocurarine[21].

Long and Bachman studied the effects of an intravenous injection of 0.1 mg/lb of d-tubocurarine in 45 children and concluded that the neuromuscular block of d-tubocurarine was related to weight and age. The younger and smaller children had a greater degree and duration of block[22]. Nightingale et al. found no relation between the magnitude of the response and the age of the child in the 13 children receiving the 0.5 mg/Kg. Children who received 0.3 mgs/Kg, demonstrated that the recovery time was indirectly related to age. The dose-response curve of succinylcholine required to decrease the action potential to 50% control decreased significantly as age increased[23].

Intraocular Pressure:

Hoffman and Holtzer reported in 1953 that succinylcholine increased intraocular pressure in unanesthetized patients to as much as 18 mm Hg. With the increased intraocular pressure, the eyes became fixed and divergent. Simultaneously with the decrease in intraocular pressure, movement returned suggesting that increased pressure might be produced by contraction of the extraocular muscles. Section of all extraocular muscles abolished the increased intraocular pressure[24]. Hexafluorenum has a number of actions which include a non-depolarizing neuromuscular blocking action, a plasma cholinesterase inhibiting effect and a functional membrane effect[25]. Although neostigmine and edrophonum are inhibitors of red cell cholinesterase, they will increase the intraocular muscle tension, hexafluorenum produces different effects. Given less than two minutes before succinylcholine, hexafluorenum prevented succinylcholine-induced increased intraocular pressure. After 20-30 minutes the magnitude of the increased pressure decreased, but the duration was prolonged[26]. Hexafluorenum may block the contraction of orbital smooth muscle and block the effects of succinylcholine-induced increased intra-orbital pressure. Miller et al. found that d-tubocurarine or gallamine infused 3 minutes prior to succinydicholine, will also prevent the increase in intraocular pressure[27].

Histamine Release:

Alam et al. after injecting curare into a limb artery of the dog found increased histamine content in the venous blood and simultaneously decreased histamine content of the muscle of the extremity[28]. Experiments in guinea pigs have demonstrated significant quantities of histamine released after intravenous d-tubocurarine[29]. Proof of histamine release in man has not been convincing, but severe episodes of bronchospasm after intravenous curare have been reported[30]. Mongar and Whelan failed to find significant increases in the plasma histamine level even after injection of 30 mgs, of d-tubocurarine[31]. Westgate et al. found that three of eleven patients showed a significant rise in histamine level accompanied by a fall in blood pressure, increased airway resistance and skin erythema[32]. Sniper found that intracutaneous injection of d-tubocurarine produced the greatest histamine release among the relaxants tested. The release of histamine by succinylcholine is about one one-hundreth of that caused by d-tubocurarine. It is wise to use small test doses of curare, injected slowly, prior to therapeutic dose and avoid curare entirely in patients with severe allergy histories.

Neomycin Interactions:

Neomycin has been used orally for intestinal antisepsis, topically for treatment of superficial infection, and, in body cavities for prevention and treatment of infection. Early investigations with neomycin in animals revealed that acute toxicity was manifested by respiratory arrest. Prolonged post-operative apnea in man following intraperitoneal neomycin reported by Pridgen, was shown to be the result of neuromuscular block[33]. Neomycin block is potentiated by diethyl ether and di-tubocurarine, succinlycholine and gallamine, but both the extent and type of pharmacological interaction remains obscure. Elmquest and Jorefsson proposed two pharmacological mechanisms for the neuromuscular blocking activity of neomycin: (a) like curare, neomycin reduces the sensitivity of the postjunctional membrane to acetylcholine, (b) neomycin inhibits release of acetylcholine from the neural end-plate an effect similar to those seen with low calcium or high magnesium concentration[34].

Reversal of the blockade can be accomplished by antagonizing the curare-like effect with a cholinesterase-inhibitor or by raising the calcium in concentration[35]. Neostigmine alone is effective only when the block is incomplete, however calcium is effective with any degree of blockade[36]. Sodium bicarbonate partially reverses complete neomycin neuromuscular block in the presence of normal pH and blood gas determinations. Sodium bicarbonate enhances the recovery produced by a low dose of calcium. The mechanism for this action is unknown.

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THE PRESIDENT'S PAGE

As we all are aware the premiums for Malpractice or Professional Liability Insurance have risen precipitously in the past year, in many instances by 100 or more per cent. Furthermore, some insurance companies have stopped offering this type of coverage. The reasons for this are quite simple according to the insurance companies; they are paying out more then they take in ($1.40 for each $1.00 received in premiums).

Professional Liability Insurance is different from other liability insurance in that the injury may not be discovered for several years after it occurs. However, the liability still exists. Thus, a physician and his insurance carrier may find themselves being sued for an act which occurred several years previous. The increase in premiums we are now experiencing is due in part to an attempt by the insurance carriers to "catch up" with this type of claim. Another phase of the problem is that there has been an increase in the number of suits filed against physicians and an increase in the amounts of the awards. Even suits that are successfully defended are costly to the insurance companies, and there may be instances where suits are settled because it is cheaper to settle them than to defend them, even successfully. This is known to plaintiff's attorneys and may contribute to the increase in the number of suits. The "contigency fee" may also play a role in the number of suits.

We in Connecticut are fortunate in that we can still obtain the insurance, albeit at higher rates. Physicians in some areas of the country are experiencing difficulty in this regard. The American Medical Association is exploring a group policy for its members and those eligible for membership. How soon this will be available to us in Connecticut is not known. The Connecticut State Medical Society as well as some of our County Associations have committees which are actively studying this problem, and hopefully will devise some solution.

It is self-evident that the simplest method of reducing professional liability costs is to reduce the number of claims and/or suits. Recognizing this, the Council, in creating the Committee on Professional Liability, included in its charge to the Committee that it conduct an educational program for physicians on ways to avoid malpractice. Properly implemented, such an educational program can reduce the number of suits. It may also serve to improve the quality of medical care.

From the deliberations of this Committee certain facts became apparent. About 80% of all malpractice claims occur for acts or injuries which occur in hospitals. Thus it would appear that some joint actions by hospital administration and medical staff should be directed towards this problem.

Another matter discussed by this Committee was the total liability program of the physician. It was felt that there was merit to the concept that the physician purchase his office liability and professional liability insurance from the same carrier, because there are instances where it is difficult to determine under which policy an injury occurring in the office setting would be covered. The purchase of "umbrella type" or catastrophic liability coverage also is advisable.

Some states, notably New Hampshire, have had a very favorable experience with professional liability. This is attributed to mandatory early reporting by the physician of all possible claims, prompt investigation and review by a committee of the State Medical Society (Peer Review) and a forceful defense of all suits where the committee has found the physician to be not at fault. The latter is undertaken regardless of how cheaply the suit can be settled. The knowledge that a suit which has no merit will be defended serves as a deterrent to such suits.

Morris A. Granoff, M.D.

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CALL
SEMI-ANNUAL MEETING OF THE HOUSE OF DELEGATES

The 1970 Semi-Annual Meeting of the House of Delegates will be held at the Hartford Hilton Hotel, Hartford, Connecticut commencing at 9:00 o'clock in the morning of Thursday, November 19.

Morris A. Granoff, President
Kenneth F. Brandon, Speaker of the House
Reginald C. Edson, Secretary

INTRODUCTION OF RESOLUTIONS

Article V, Section 12, Par. 3 of the Bylaws of the Society Provides that:

All resolutions to be considered as regular business at any regular meeting of the House of Delegates must be in the hands of the Speaker not later than seventy-two hours before the opening of that meeting. All resolutions and recommendations published in the official agenda distributed to the members of the House prior to the meeting at which action is to be taken shall be considered as regular business. Resolutions presented later than seventy-two hours before the opening of a meeting will be referred for consideration as regular business by the House only when they are presented by the Council or accepted for consideration by majority vote of the delegates present. Any resolution which does not qualify in accordance with the aforesaid provisions for consideration as regular business may be accepted for action by a majority vote of the delegates present and, if so accepted, shall be referred at once by the Speaker to a reference committee. Any such reference committee shall consider resolutions referred to it and shall report, with recommendations to the House before adjournment of the meeting.

Proposed Amendments to the Bylaws

The following proposed amendments to the Bylaws were presented to the House of Delegates on May 12, 1970 and were tabled for consideration and action at the next regular meeting of the House of Delegates.

In accordance with the Bylaws, these amendments will be published in Connecticut Medicine, "on one or more occasions prior to the next meeting. . . . at which meeting the amendments shall be taken off the table and acted upon by the House of Delegates."

Introduced by the Council

Purpose: To delete the "Advisory Committee to the State Board of Examiners for Nursing"

Amendment

Article XI—Divisional Boards and Committees

Section 3—Divisional Standing Committees

(A) Education and Hospitals Division

Amend by deletion of "Advisory Committee to the State Board of Examiners for Nursing"

Section 5—Duties of Standing Committees

Amend by deleting *Par. 1—Advisory Committee . . .* for Nursing in its entirety.

Renumber succeeding paragraphs of Section 5 appropriately.

Recommended by the Fairfield County Medical Association.

Approved by the Council on April 29, 1970.

Purpose: To make AMA Alternate Delegates voting members of the Council.

Amendment

Article VI—General Officers

Section 1—Designations (Add the underlined words)

The general officers of The Society shall be a President, a President-Elect, a Vice-President, a Secretary, a Treasurer, a Speaker of the House of Delegates, a Vice-Speaker of the House of Delegates and the Delegates *and Alternate Delegates* to the American Medical Association.

SUMMARY OF ACTIONS
COUNCIL MEETING
Thursday, August 13, 1970

I. Attendance

Present in addition to the Chairman, Dr. S. J. Martin, and the Vice-Chairman, Dr. K. F. Brandon, were: Drs. Granoff, Weber, Jr., Grendon, Edson, Abbot, Fabro, Cramer, McDonald, Harwood, Pelz, Palomba, Roch, Nemoitin, Friedberg, Freedman and Root, Jr.

Also present were: Mrs. Lindquist, Mr. Donelan (AMA), Mr. Gordon (HCMA), Dr. Patterson (Dean, UConn Medical School), Dr. Hess, (Welfare Medical Director), Mr. Tomat, Mr. Sullivan and Dr. Richards.

Absent were: Drs. Burnham, Dean, Gardner, Rem, Wilson, Jr., VanSyckle, Johnson, Ragland, Gorin, vonGlahn, Purnell and Klare.

In Memoriam: Ellwood C. Weise, Sr.

Having been apprised of the death of Ellwood C. Weise, Sr., of Bridgeport, on July 18, 1970, the Council members observed a moment of silent prayer in his memory and, thereafter, adopted a memorializing resolution as follows:

"WHEREAS: Ellwood C. Weise, Sr., Bridgeport, had a long and distinguished career as a practitioner of medicine and achieved national and international recognition in his chosen field of Dermatology, and

WHEREAS: He contributed unstintingly of his time and energies to the betterment of medical practice and the public health as an actively participating member of the Fairfield County Medical Association and of the Connecticut State Medical Society, serving the latter as President, Councilor-at-Large, and Alternate Delegate and Delegate to the American Medical Association; therefore be it

RESOLVED: That the members of the Council of the Connecticut State Medical Society note with sorrow the passing of a distinguished colleague and valued friend, Dr. Ellwood C. Weise, Sr., of Bridgeport, on July 18, 1970, and honor his memory by a period of silent prayer; and be it further

RESOLVED: That this expression of tribute and respect to Dr. Weise, Sr. be spread upon the minutes of this meeting of the Council, August 13, 1970, and that notice thereof be transmitted to the members of his immediate family."

II. Routine Business

Approval of Minutes

As printed and distributed, it was VOTED to approve the minutes of the meeting of July 15, 1970.

Life Memberships

It was VOTED to approve applications for Life Membership received from the following eligible Active Members:

Clifford D. Moore, 501 High Ridge Road, Stamford (FCMA)—1970

Mario L. Palmieri, 200 Coleman Road, Middletown (MCMA)—1/1/71

Lewis Sears, 14 Julian Street, Norwich (NLCMA)—1/1/71

Roland T. Wehger, 158 Plymouth Avenue, Trumbull (FCMA)—1970

Date of Next Meeting

The next meeting of the Council is scheduled for Wednesday, September 16, 1970.

III. Old, New and Special Business

Communication—Committee on Program of Scientific Assembly

Filing a brief memorandum with the Council concerning membership attendance at the Scientific Assemblies in recent years, the Committee suggested that the Council might consider making attendance at one Scientific Assembly in (perhaps) a 3-4 year period a requirement for continued membership in good standing. Following thorough discussion, it was VOTED *not* to approve the suggestion offered by the Committee.

Report—Committee on National Legislation

It was VOTED to accept as information a written report submitted by Bernard A. Burnham, Committee Chairman, which described the activities of a delegation of CSMS representatives during a two-day "Congressional contact" visit to Washington, D.C., July 22-23, 1970; also, a brief supplementary verbal report by James H. Root, Jr. which described the matters discussed by several members of the delegation with representatives of the Department of Health, Education and Welfare.

Registrations, Appointments, Etc.

(a) *Committee on Aging:* It was VOTED to accept with regret, and thanks for past service, the resignation of Alexander J. Tutles, Hartford, as Chairman and as a member of this Committee. It was further VOTED to appoint Seymour H. Saltzman, Hartford, to replace Dr. Tutles as Committee Chairman.

(b) *Committee on Postgraduate Education:* It was VOTED to appoint Gordon K. MacLeod, New Haven, to membership on this Committee.

Minutes—Meeting, CSMS-CG Liaison Committee re Medicare B Progress Report—Coordinating Committee on U&C Charge Programs

Because of considerable intermeshing of the subject matters of these two items, they were considered and acted upon as one.

(a) *CSMS-CG Liaison Committee:* It was VOTED to accept as information the minutes of the meeting of this Committee on July 27, 1970. In the discussion of this item that ensued, the thought was expressed that the Liaison Committee may have outlived its usefulness and relevancy and that perhaps it should be disbanded, replaced or combined with another committee (such as the Coordinating Committee on U&C Charge Programs) in order to achieve a more effective, formal mechanism for providing "peer review" with respect to the Medicare B. Program. However, no action is to be taken in this regard at this time.

(b) *Coordinating Committee:* In a progress report submitted by Sidney L. Cramer, Committee Chairman, it was brought out that while the Committee has been making some exploratory studies of the feasibility of establishing "criteria" by which to judge proper utilization of physicians' services in the various fields of practice, it may be that such a project is not feasible unless it is coordinated with some committee for utilization review which has statewide jurisdiction. Dr. Cramer voiced the thought that, in light of pending Federal legislation, perhaps this Committee, also, should be disbanded, replaced or combined with another committee to the end that plans for a "statewide" review committee might be made. As in (a), no action is to be taken in this regard at this time.

(c) *Study Committee:* Stemming from the discussions of items (a) and (b), it was VOTED to appoint Kurt Pelz, Chairman of the Liaison Committee with CG, and Sidney L. Cramer, Chairman of the Coordinating Committee on U&C Charge Programs, as a "committee of two" to draw up a plan for possible amalgamation of their respective committees and the charge to be given to such an amalgamated committee.

Legislative Proposals—Kidney Foundation of Connecticut

Joining the Council to present and discuss a series of legislative proposals concerning facilities for treating patients with advanced renal damage were Dr. John Goffinet, Chairman of the Medical Advisory Board of the Kidney Foundation of Connecticut, and Dr. Bernard Lytton, Associate Professor of Urology at the Yale School of Medicine. The proposals were general in nature, but were directed to the establishment of a State Commission which would provide coordinative and consultative services for persons suffering from renal insufficiency, and advisory services to agencies and facilities desirous of setting up dialysis units or operating homecare therapy programs. It was VOTED to receive the proposal and comments of Drs. Goffinet and Lytton as information, and to await further communication (sample bills, etc.) from them before turning the matter over to the Committee on State Legislation for appropriate action.

Date and Place—1970 Semi-Annual Meeting, House of Delegates

(a) It was VOTED to invite the Hartford County Medical Association to serve as "host" Association for the meeting, and to assist the CSMS staff in the selection of an appropriate facility in Hartford County at which to hold it.

(b) It was VOTED to hold the meeting during the week of November 16, 1970, with the day of the week to be set as follows:
First choice: Thursday, November 19; Second choice: Wednesday, November 18; Third choice: Tuesday, November 17.

Medicaid Program

Without formal action, the matter of appointing a Medical Advisory Committee was taken from the table and a list of nominees developed. The list contained nominations made by several of the County Medical Association, nominations of members who had served previously with the Title XIX Medical Advisory Committee in 1968-69, and several nominations from the floor. It was then VOTED to submit the list, as prepared, to the Commissioner of Welfare for his selection of the members of the MAC that he will appoint, noting only (by asterisk) the members who had served with the MAC during the "usual and customary charge" trial year. It is the Council's understanding that, when the Committee has been appointed, the members of the Committee will elect their chairmen (as did their 1968-69 predecessors).

It was clear from the discussion and review of the details of the new program that a few minor problems will have to be gotten rid of before the program can operate smoothly. However, Dr. Hess

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is of the opinion that if practitioners will execise reasonable patience and forbearance, the program can be "phased in" without undue difficulty.

N.B.: *The foregoing is a summary of the proceedings and action of the Council on August 13, 1970. Detailed minutes of the meeting are on file at 160 St. Ronan Street, New Haven, for perusal by any interested member of the Society.*

Placement Wanted

GENERAL PRACTICE—32 years of age, with National Boards, wishes group type practice in Connecticut. Available in November when military obligation completed. Contact: Lee M. Dippery, Major, MC, M.D., H.Q. 6/10 Field Artillery, New York APO 09139.

FAMILY PRACTICE—55 years of age, Certified with National Boards, wishes group or institutional type practice in Connecticut. Available immediately.

GENERAL PRACTICE—30 years of age, wishes solo, associate or institutional type practice in a small community in Connecticut. Military obligation completed.

GENERAL PRACTICE—59 years of age, Eligible with Connecticut license wishes group, associate, institutional or industrial type practice in Connecticut. Available immediately.

INTERNIST – ENDOCRINOLOGY – 33 years of age, Eligible with National Boards. Prefers to practice internal medicine-endocrinology in a group or with associate, but must affiliate with university-type teaching hospital. Military obligation completed. Available immediately.

INTERNIST—38 years of age, Eligible wishes group or industrial type practice in Connecticut. Will consider any position. Connecticut license. Presently available. Contact Declan Foley, M.D., 76 North Pearl Street, Meriden, Connecticut 06450.

INTERNIST—46 years of age, Certified with National Boards, wishes group, institutional or industrial type practice in Connecticut. Presently in practice. Connecticut license. Available immediately.

INTERNIST—34 years of age, Eligible, wishes associate or institutional type practice in Connecticut. Presently in practice.

INTERNIST—33 years of age, Eligible with National Boards, wishes group, associate or institutional type practice in a large or medium size community in Connecticut.

NEUROSURGERY—32 years of age, Eligible with National Boards, wishes solo or associate type practice in Connecticut.

OBSTETRICS & GYNECOLOGY—33 years of age, Eligible with National Boards, wishes group type practice in a medium size community in Connecticut. Presently in practice. Military obligation completed. Contact: Stephen B. Berkowitz, M.D., 415 Grand Street, Apt. 1801, New York, New York 10002.

PATHOLOGIST—39 years of age, Certified with National Boards, wishes associate type practice in a medium size community in Connecticut. Connecticut license. Desires position as chief Pathologist or laboratory director. Contact: Sanford H. Edberg, M.D., Lee Hospital, 320 Main Street, Johnstown, Pennsylvania 15901.

PATHOLOGIST—31 years of age, Certified with National Boards, wishes group, associate or institutional type practice in a large or medium size community in Connecticut. Available immediately.

PATHOLOGIST—35 years of age, with National Boards, wishes group, associate or institutional type practice in Connecticut.

PEDIATRICIAN—47 years of age, Certified, wishes group or associate type practice in a large or medium size community in Connecticut. Presently in practice.

PEDIATRICIAN—33 years of age, Certified, wishes solo, group, associate or institutional type practice in a large or medium size community. Academically oriented practice prefer medical school affiliation. Available immediately.

PEDIATRICIAN—40 years of age, Eligible, wishes solo, group or associate type practice in a medium or small size community in Connecticut. Available immediately. Contact: Vasant G. Yadav, M.D., 201 W. Cuthbert Blvd., Oaklyn, New Jersey 08107.

PEDIATRICIAN—35 years of age, Certified, wishes group, associate or institutional type practice in Connecticut. Available immediately.

SURGEON—33 years of age, wishes group or associate type practice in Connecticut. Certified with National Board. Available immediately.

Placement Opportunities

ANESTHESIOLOGIST—position available for associate to board-certified anesthesiologist in an attractive progressive general hospital. Excellent staff. Generous remuneration. Minimum amount of call with maximum vacation time. Write or call: Dr. Marvin Albert, World War II Veterans' Memorial Hospital, Paddock Avenue, Meriden, Connecticut 06450. Telephone 203-237-5531.

DISTRICT HEALTH DIRECTOR for Westport/Weston, Connecticut. Requires M.D., degree in Public Health or equivalent experience, and eligibility for Connecticut license. Salary range $22,000 to $26,000 depending on qualifications. Population served, 35,000. Excellent schools cultural and recreational opportunities. Position available October, 1970. Send resume to Clifford W. Mills, M.D., Chairman, Aspetuck Valley Health District Board, 180 Bayberry Lane, Westport, Connecticut 06880.

OPPORTUNITY FOR INTERNIST OR GENERAL PRACTITIONER for association with General Practitioner. A good family practice in urban community in Connecticut. No Ob or major surgery. Part-time University position if desired.

PATHOLOGIST ASSISTANT—Board qualified or eligible. Attractive newly established position available in a progressive 320 bed accredited general hospital located in beautiful Southern Connecticut. Clinical and anatomic pathology. Expanding hospital laboratory with approved school of medical technology. Salary open, excellent benefits. Please send curriculum vitae to: Gilles Allard, M.D., Pathologist, Director of Laboratories, St. Joseph's Hospital, Stamford, Connecticut 06904.

PATHOLOGIST—Board certified AP-CP with 3-5 years experience, to associate with director of modern laboratory in accredited voluntary hospital nearing completion of expansion to 400 beds. Active teaching program for interns and residents; medical school affiliation. Write: Dr. I. Rothstein, Mount Sinai Hospital, Hartford, Connecticut 06112.

PEDIATRICIANS—Two board certified Pediatricians seek dynamic young associate to join rapidly expanding practice and medical community for the general practice of Pediatrics. Excellent salary to partnership. Equal time off. No investment necessary. For further information contact: Thomas J. McGrath, M.D., 108 New London Turnpike, Norwich, Connecticut 06360. (203) 889-3835.

PEDIATRICIANS—Two Pediatricians are needed to serve a growing community of over 50,000 people. Area consists of several small towns with population of 3,000 to 14,000 each. Good country living with easy access to larger cities via well developed highway system. Community hospital is now expanding and more physicians are needed. Contact: E. B. Raheb, Chief of OB & GYN, Day Kimball Hospital, Putnam, Connecticut 06260.

PEDIATRICIANS—At least two pediatricians are needed for private practice to serve a growing community of over 50,000. Area consists of several towns with 3,000 to 14,000 population each. Good country living with easy access to major cities via well developed highway system. Contact: Edmond B. Raheb, M.D., Chief of OB-GYN, Day Kimball Hospital, Putnam, Connecticut. (203) 774-5151.

PEDIATRICIANS—opportunity in area of 75,000 for hospital-based private practice or community-based private practice. Modern 250 bed, Yale affiliated, general hospital in Southern Connecticut suburban community. Excellent diagnostic services available. Attractive living conditions. Reply to: Administrator. Griffin Hospital, Derby, Connecticut 06418.

PHYSICIANS AND RESIDENT PHYSICIANS—opportunities with the State of Connecticut in medical hospitals, institutions for the mentally retarded, and Veterans' Home and Hospital. Residencies $10,694-$16,110; Physician $17,760-$21,960; Senior Physician $19,303-$23,755; Maternal and Child Health Physician $21,002-$25,700; Medical Consultant $21,002-$25,700; Internist $21,911-$26,729; Chief, Epidemiology Section $21,911-$26,729. Excellent benefits. For further information contact Mr. John Crowley, Agency Personnel Administrator, Department of Health, 79 Elm St., Hartford, Connecticut or Mr. Edmund Buetsch, Personnel Officer, Veterans' Home and Hospital, Rocky Hill, Conn.

PHYSICIANS—Five room office fully equipped with X-ray and laboratory. Located in beautiful Southern Connecticut shoreline area. Six blocks from Community Hospital, which is expanding. The hospital is the only one within 45 mile radius. Community over 40,000 people which consists of several small towns with population 3,000 to 14,000 each.

CONNECTICUT-SENIOR PSYCHIATRISTS—In a 3 year accredited dynamic, decentralized community-oriented mental hospital. Affiliated with Yale University, Wesleyan University, and University of Connecticut. Excellent opportunities for professional growth and advancement. Starting salary range $19,303-$26,986, depending on experience and training. Liberal benefits. Eligibility for Connecticut license required. Send all particulars in first letter, including references to Mehadin K. Arafeh, M.D., Superintendent, Connecticut Valley Hospital, Box 351, Middletown, Connecticut 06457.

PSYCHIATRISTS AND PSYCHIATRIC RESIDENTS—Openings in the mental hospitals and mental health clinics of the State of Connecticut. Residencies, $10,694-$16,110; Psychiatrist I, $19,303-$23,755; Psychiatrist II, $20,128-$24,700; Psychiatrist III, $21,911-$26,729. Excellent benefits and opportunity for advancement. For further information contact Mr. Robert Tacey, Agency Personnel Administrator, Department of Mental Health, 90 Washington Street, Hartford, Connecticut.

OBSTETRICS & GYNECOLOGY—Board eligible or rated, to immediately take over 20 year successful solo practice. Coastal Fairfield County. Token investment. Will introduce if available. Connecticut license required. Must be available soon. Incumbent leaving area permanently. Lease available.

ASSOCIATE RADIOLOGIST—N.E. Connecticut. 180 Bed Community Hospital. Near large State University. 50% Medical Staff Board Certified Specialist. Moving to new 9 room Department near future. Early partnership. Locums accepted until postion is filled. E. Herbert, M.D., Windham Community Memorial Hospital, Willimantic, Connecticut.

The Connecticut State Medical Society offers placement assistance through the Physician Placement Service, 160 St. Ronan Street, New Haven, Connecticut, 06511. This service is for the use of physicians seeking locations as well as physicians seeking associates, and is without charge.

ANYONE INTERESTED IN THE ABOVE IS ASKED TO CONTACT THE EXECUTIVE DIRECTOR'S OFFICE, 160 ST. RONAN STREET, NEW HAVEN, CONNECTICUT 06511.

Commission on Emergency Medical Services AMA

(*Bull. Amer. Coll Phys.* 11, 283, June 1970, Schnitker, M.A.) A Commission on Emergency Medical Services of the AMA held a meeting in Chicago on April 16, 1970. A brief discussion was held concerning categorization of Emergency Medical facilities in local communities which must include (a) the scene of the accident, (b) transportation, (c) communication, (d) hospital emergency room, (e) back-up services in the hospital.

There were different outlines being developed by numerous organizations which will be reviewed by a central body.

An outline of a program developed in northwestern Ohio was presented by Dr. Schniker for the Council on Emergency Medical Services including 20 counties, 42 hospitals made up with 31 categories. Copies were made for distribution to all members of the Commission.

To bring together a common understanding of this broad and vital subject, a conference is projected for sometime in the fall of this year.—L.H.N.

PERINATAL SEMINAR

Sponsored by

Connecticut State Medical Society
Yale University School of Medicine
Connecticut State Department of Health
American Academy of Pediatrics

WEDNESDAY, NOVEMBER 18, 1970

9:00 A.M. — 4:30 P.M.

Yale-New Haven Medical Center
Harkness Auditorium
333 Cedar Street
New Haven, Connecticut

Anesthesiology Grand Rounds
Yale-New Haven Hospital
The Hypoxic Mother in Labor

Samuel M. Lerner, M.D. and Frederick W. Hehre, M.D., Editors
John C. Daniels, M.D., Ruth Whittemore, M.D.* and Robert Hook, M.D., Discussants

Dr. John C. Daniels:

The patient was born in 1949 following an uneventful pregnancy and a normal, full term, spontaneous delivery. Birth weight was 7 lbs. 2½ oz. Physical examination at that time was within normal limits. Cyanosis with crying was first noted at one month, and at the six week checkup, a heart murmur was first heard. During the next 4 years, she developed increasing exertional dyspnea, easy fatigability, constant cyanosis and squatting, as often as 4-5 times per day, when tired. The presumptive diagnosis was tetralogy of Fallot. Growth and development was in the low, normal range.

At age 5, the patient underwent cardiac catheterization and the diagnosis of tetralogy of Fallot was confirmed. She underwent a five hour pulmonary-subclavian artery anastomosis under nitrous oxide-meperidine-curare anesthesia. She was discharged 19 days later, after a benign post operative course. The patency of the shunt was evidenced by a significant decrease in cyanosis and increase in exercise tolerance.

During the next 10 years, she was seen at six months, and then yearly intervals. The shunt remained patent and she developed cyanosis only with strenuous exercise. Her hematocrit was stable in the range of 50-55. Her EKG also remained stable, showing right ventricular hypertrophy and first degree heart block. Growth and development remained in the low normal range.

In August 1965, at the age of 15, she was admitted to Yale-New Haven Hospital with subacute bacterial endocarditis due to alpha streptococcus which was treated with penicillin successfully. She had had minor dental work without penicillin coverage one month prior to the onset of symptoms. The only complication was two minor episodes of pulmonary embolization.

For three years she exhibited good exercise tolerance, minimal cyanosis, and stable hematocrit and electrocardiogram. In May 1968, she had a second episode of subacute bacterial endocarditis due to alpha streptococcus, and she was again treated with penicillin for six weeks and made an uneventful recovery.

In November 1969, she was scheduled for cardiac catheterization for evaluation for total corrective surgery, but she announced that she was 15 weeks pregnant, and plans were cancelled. Her EDC was April 17, 1970. She was followed at two week intervals without evidence of congestive failure, and her hematocrit remained in the high 40's. Urinary estriol levels were first measured at 30 weeks gestation, and remained at levels below normal. (Urinary estriol levels are a measure of placental competance —Ed.) Uterine size and estimated fetal size were abnormally small.

From the 33rd week of gestation there was no increase in uterine or fetal size and no increase in estriol levels. The decision was made to admit her to the hospital, place her on bed rest and give oxygen supplementation, in the hope that this regime would increase arterial oxygen tension and stimulate fetal growth. Blood gases on admission were: pH 7.46; pO_2 53; pCO_2 14.5 and O_2 saturation 88.5%. During the next two weeks, the urinary

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DR. SAMUEL M. LERNER is Assistant Clinical Professor of Anesthesiology, Yale University School of Medicine.

DR. FREDERICK W. HEHRE is Associate Professor of Anesthesiology, Yale University School of Medicine.

DR. JOHN C. DANIELS is Associate Clinical Professor of Anesthesiology, Yale University School of Medicine.

DR. RUTH WHITTEMORE is Clinical Professor of Pediatrics, Yale University School of Medicine.

DR. ROBERT HOOK is Assistant Clinical Professor of Anesthesiology, Yale University School of Medicine.

From the Division of Anesthesiology and the Department of Pediatrics*, Yale University School of Medicine and The Departments of Anesthesiology and Pediatrics*, Yale-New Haven Hospital, New Haven, Connecticut.

estriol levels rose, though not to normal levels, and uterine height increased three centimeters.

At 39 weeks gestation, urinary estriol levels fell, and she was given a "stress test" with intravenous oxytocin. She began to have contractions immediately but progress was slow, and she was rested overnight. Induction was begun again the following morning and by evening she was in active labor. At 6:00 P.M. she was given meperidine 50 mg intramuscularly and at 6:30 P.M. fetal membranes were ruptured artificially. At 8:30 P.M. continuous lumbar peridural anesthesia was instituted with an initial dose of 7 cc of 2% lidocaine (140 mg) with 1:200,000 epinephrine which produced a sensory level of T10-S5 after 15 minutes with complete relief of pain. Her initial blood pressure of 140/80 mmHg fell to 100/60 mmHg after 10 minutes. She was turned on her left side and the blood pressure rose to 110/70 mmHg and remained at this level. She was taken to the delivery room for monitoring purposes and given O_2 by mask intermittently. At 10:00 P.M., the peridural anesthesia was reinforced with 5 cc of 2% lidocaine (100 mg) with 1:200,000 epinephrine with complete pain relief. At 10:30 P.M. a cord compression pattern was noted on the fetal electrocardiogram (Fig. I). She was given oxygen by mask. At 10:45 P.M. a fetal heart rate of 60 was noted. Vaginal examination revealed prolapse of the umbilical cord. Low forceps were applied and a 1780 gram female infant delivered at 10:48 P.M. The Apgar Score at one minute was 8; at five minutes 9. The baby was suctioned with bulb and mucous trap and given oxygen by mask. No abnormalities, other than small size were noted.

Lochia was excessive after delivery, and four hours postpartum she became hypotensive, with blood pressure 80/50 mmHg. Her hematocrit had fallen from 47 percent prior to delivery to 37 percent. She was given one unit of packed red blood cells and one unit of whole blood and her blood pressure returned to normal. Despite lack of evidence of external bleeding, her hematocrit continued to fall, and reached 32 percent on the fourth postpartum day. The reticulocyte count was 2.7%, but the red cell indices, prothrombin time, platelet count and partial thromboplastin time were within normal range. She received two additional units of packed cells. Multiple blood cultures were nega-

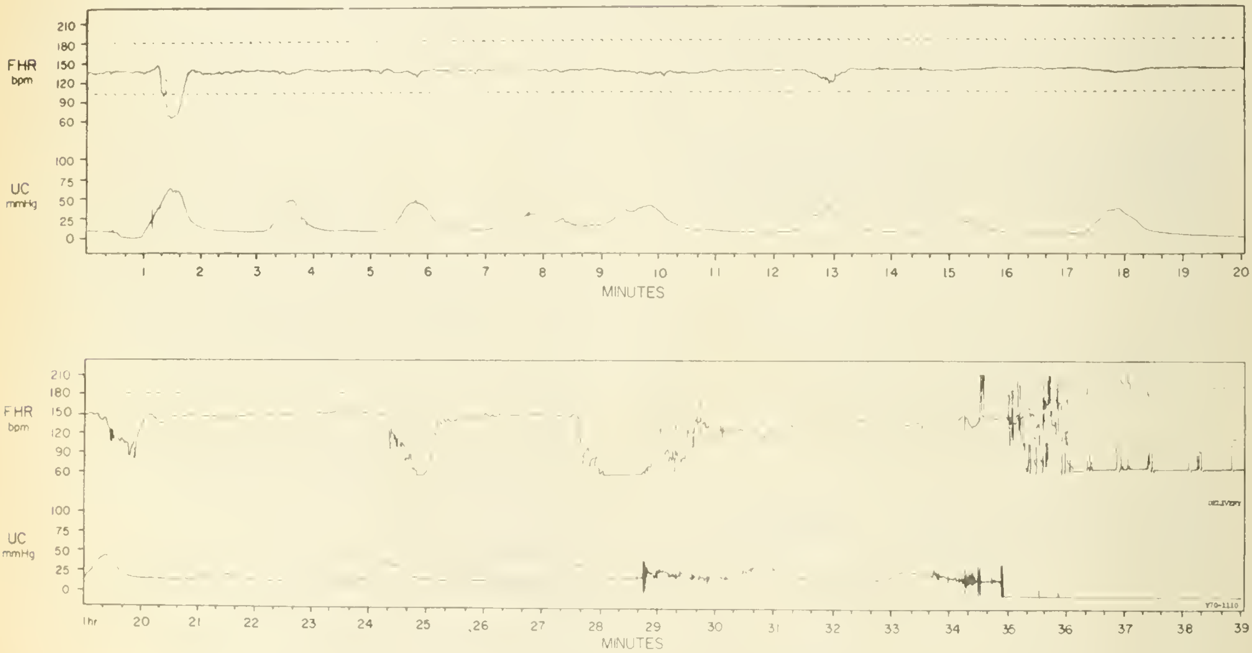

Figure 1

FHR — fetal heart rate; UC — uterine contractions, or, intraamniotic fluid pressure.

The upper trace was taken during the early stage of monitoring in the delivery room and shows a normal baseline at approximately 130 beats per minute, with the exception of one variable decelleration pattern between minutes 1 and 2.

The lower trace shows the last 20 minutes of labor including delivery. Three increasingly more severe variable decelleration patterns are noted. Between minutes 29 and 35, the fetal heart rate baseline returns to normal. The heart rate dropped to 60 or less after minute 35 which was associated with the application of forceps and delivery.

tive. She was discharged on the 8th postpartum day. The baby was discharged two weeks later having attained a weight of 2300 grams. At 6 weeks postpartum, mother and baby were doing well.

Dr. Samuel M. Lerner: Dr. Whittemore, would you please comment on the effect of tetralogy of Fallot on this pregnancy.

Dr. Ruth Whittemore: Primarily we are dealing with a hypoxic mother. This patient had an oxygen tension both before and after the pregnancy, in the 52-54 mmHg range. The pCO_2 was as low as 14 mmHg in the second and third trimesters but was 20 mmHg at delivery. It has risen to 28 since delivery. We are aware that in the Andes Mountains, infants born to naturally hypoxic mothers are, as a rule, small for gestational age. Why? Is it due to hypoxia? We wonder whether hypoxia alters the endocrinological picture in these pregnant women. That is, do they have as good an endocrinological response as normal women?

A series of infants born to cyanotic mothers was studied at Johns Hopkins by Neill and Hellegers[1, 2]. The mothers were divided into 3 groups according to the degree of polycythemia, which is considered a manifestation of the severity of hypoxia. About half of the women whose hemoglobin was 15 grams or less and hematocrit of 45% or less predominantly gave birth after 38 weeks of gestation to infants weighing more than 2500 grams or more, the remaining infants being slightly smaller than expected for gestational age. In mothers with hemoglobin of 15-18 grams and hematocrit of 45-60%, almost all infants were small for gestational age, and there were many fetal losses. When the hemoglobin was above 18 grams and hematocrit was over 60%, fetal loss approached 100%, the majority under 20 weeks gestation.

What happens to live-born infants of cyanotic mothers? Do they make up for lost time once they leave the uterus? At what stage of fetal development does the maternal hypoxia become critical? None of these questions have been adequately studied. We have observed 14 live infants born of cyanotic mothers. They were small at birth and lose weight neonatally, as do all infants. But once these children start to gain weight, the majority gain more rapidly than expected. The one that drew my attention to this problem was a baby who weighed 1250 grams at birth and lost very little weight and started to gain such that she crossed the percentile line so rapidly that after 50 days she weighed 5½ lbs. instead of under 4 lbs. 12 oz. as expected. The majority have growth curves on the premature weight chart a little better than expected. This has been the case with this patient's baby. At 2 months, her baby weighs 7 lbs. 11 oz. She has almost doubled birth weight in the first 2 months of life.

In 14 patients with congenital cyanotic heart malformation we have observed 20 pregnancies: 14 live infants, 3 miscarriages, and 3 had therapeutic abortions. Of the 14 live infants, 9 have shown low birth weight for gestational age. Only 5 infants born to 4 mothers were of adequate size. Two mothers had total correction of tetralogy of Fallot and one had a Blalock anastomosis at the age of 6. The fourth had a valvulotomy for pulmonary stenosis and atrial septal defect which had previously permitted right to left shunting. Two of these infants were over 3 lbs. but this mother, who had had total correction, had developed diabetes. In general, we have the impression that mothers who have had corrective surgery can give birth to a normal sized infant. There was one infant who did not fit into this group. This mother resembled this afternoon's patient. She had almost the same pO_2, but a little bit more polycythemia. Her urinary estriols were normal and she delivered a normal 6 lb. 5 oz. infant at the 41st week of gestation. This is the only one who had only a palliative Blalock operation who delivered a normal sized infant.

The tendency of these cyanotic patients to abort is much higher than the normal population. If we can prolong the pregnancy to get a viable infant, they will be small infants for gestational age who make up for lost time once they leave the uterus, and rarely have complications.

Dr. Nicholas M. Greene: What are the figures for maternal morbidity and mortality?

Dr. Whittemore: We have not lost any mothers in the postpartum period; nor were any lost in the immediate postpartum period in the Hopkins study. There have been one or two cases who were inadequately covered with antibiotics and developed endocarditis. The one late death possibly associated with bacterial endocarditis and a brain abscess occurred many years ago. One mother with severe pulmonary hypertension died 8 years later.

Dr. Greene: So the problem is more one of prematurity.

Dr. Whittemore: Yes. A better term is small-for-gestational age.

Dr. Marc D. Rosenberg: How about congestive heart failure?

Dr. Whittemore: We have not seen failure in these patients. The increased blood flow and blood volume which result from the pregnancy does not seem to bother them, probably because the shunts were small for these patients who are now adult size. There have been changes in the intensity of the continuous murmur of a functional Blalock anastomosis, but no evidence of congestive failure in any of these particular patients.

Dr. Lerner: Dr. Hook, would you discuss the anesthetic considerations in the management of these patients during labor and delivery.

Dr. Robert Hook: There are three factors of prime importance in the anesthetic management of pregnant females with congenital cyanotic heart disease:

(1) Effective pain relief must be provided early in labor to reduce the amount of work imposed on the patient's heart and decrease her oxygen demand.

(2) Prevention of shunt reversal and severe hypoxia by avoiding hypotension, respiratory obstruction, and eliminating the urge to bear down.

(3) Avoidance of any drug induced myocardial depression.

Several alternatives which fit these criteria are available to the anesthesiologist. The optimal use of doses of sedatives and narcotic analgesics during the first stage of labor combined with inhalation analgesia and paracervical block for delivery is one suitable approach. But the disadvantages of this technique include: (1) The difficulty inherent in determining the optimal dose of a narcotic for any given patient. In many patients an analgesic dose of a narcotic is sufficient to cause respiratory depression and a large dose may also have a profound effect on the fetus.

(2) Paracervical block for the second stage with inhalation analgesia for delivery is not without danger. Rapid absorbtion of local anesthetic drug has been reported to cause fetal bradycardia. In our hands this combination is not reliable.

In our opinion, the technique which best meets the requirements is continuous lrmbar peridural anesthesia. When administered by the low dose technique in the accelerated phase of first stage, peridural block provides early analgesia, a relaxed patient, abolishes the bearing down reflex and has minimal effect on the fetus. It usually requires no inhalation supplementation at delivery and, in our experience, the incidence of hypotension, if attention is direct to positioning and replacement of intracellular fluid volume, has been minimal.

Discussion:

Dr. Joseph Guaraldo: Were most of the patients mentioned in this study anesthetized with peridural anesthesia?

Dr. Hook: I know that three were, and all were without incident. I do not know the details of the other patients' management.

Dr. Greene: It was mentioned that this patient was admitted to the hospital and given oxygen in an attempt to increase the size of the fetus. How was the oxygen administered?

Dr. Daniels: By tent.

Dr. Greene: The patient was inhaling only 40 or 50% oxygen. I was interested in what might have happened to the lungs if you had given 100% oxygen by mask for such a long period of time.

Dr. Whittemore: We were confronted with low urinary estriol levels and an infant that had suddenly stopped growing. We thought that this might be due in part to hypoxia. We know that we can increase the fetal oxygen tension by giving oxygen to the mother, since there was nothing to lose and possibly something to gain, placed her in an oxygen tent about half of the time at 40% concentration. We were mindful not to give high oxygen concentrations by mask. We did not have alteration of urinary estriols that was really significant. Bed rest alone could have augmented the estriols. But the estimate of fetal size indicated an estimated increase of a pound in this baby's weight in that two week period.

Dr. Greene: I think that it is interesting since the primary problem here is related to fetal prematurity rather than to maternal risk, that this is why the tendency is to have them deliver from below rather than by elective Caesarean section. The problems of prematurity would be made worse if section were routinely relied upon.

Dr. Luke M. Kitahata: Do those infants have a compensatory polycythemia?

Dr. Whittemore: They have quite a polycythemia. This infant's hematocrit was 72% at 12 hours of age, and the hemoglobin was 23. Over the next 19 days, hematocrit fell to 51% and hemoglobin to 17 grams. Since then the baby has looked perfectly normal with hemoglobin of 14 grams. During labor we measured the fetal scalp and maternal arterial oxygen saturations simultaneously. The pO_2 of the fetal scalp was 17 mmHg with a maternal pO_2 of

60 mmHg. At birth, the umbilical artery pO_2 was 24 mmHg; at 15 minutes 60 mmHg; and, at 30 minutes 73 mmHg which was a very good rise.

Dr. Frederick W. Hehre: The fetal scalp pO_2 was very definitely in the borderline area. A fetal pO_2 in that range would suggest uteroplacental insufficiency. But the fetal electrocardiogram does not show late decelleration changes, but rather the heart rate is within normal range until near the end when variable decelleration patterns of cord compression are evidenced by the bradycardia (Fig. I). The prolapsed cord at delivery produced the final rate of 60.

Dr. James Drews: I am not surprised at the discrepancy between the fetal and maternal oxygen tensions with the pCO_2 in that range. The fetal hemoglobin dissociation curve is to the left of the maternal curve. With a pCO_2 of 14 mmHg, the maternal would shift over almost to the fetal and would limit the amount of oxygen transferred from the mother to the fetus.

Dr. Whittemore: The hemoglobin-oxygen dissociation curve was performed on this baby and the mother. The mother's curve was shifted well over to the right, as indicated by a P50 value of 28.1 (normal 25.8 ± 1.1). The P50 of the infant's dissociation curve was 20.5 (normal for the gestational age). This represents oxygen affinity by measurement of the partial pressure of oxygen at 50 percent saturation (P50) at a temperature of 37°C. and a pH of 7.4.

Dr. Greene: Her pH was 7.46 so that although the pCO_2 was 14 mmHg, she had compensated. The effect of pCO_2 (the Bohr effect) on the oxygen dissociation curve is related to pH, not to the pCO_2 per se.

The other thing that occurs to me is that there are people who normally live with arterial oxygen tensions in the 50's. It is my understanding that these people, although they do have smaller infants, do not have infants who are small for gestational age as great as that represented in this case. This problem of low birth weight is not as great among the inhabitants of the Chilean and Peruvian Andes as it is in the presence of cyanotic heart disease. The point I am making is that I am not sure that all the effects of tetralogy of Fallot are only due to decreases in oxygen tension. A person at altitude may have equal decreases in oxygen tension but physiologically react in a completely different manner.

An interesting example of this is, as we reported some years ago, that a patient with congenital cyanotic heart disease shows metabolic evidence of anoxia, particularly changes in lactate-pyruvate ratio, to a degree one would expect in a normal person if subjected to hypoxia. On the other hand, a patient at altitude in the Andes shows metabolic adaptation to the hypoxia and does not have equal changes in lactate-pyruvate ratios. The difference is due not to differences in pO_2, because the pO_2 is the same, but to differences in peripheral blood flow and cardiac output.

Dr. Su-Ryong Hur: Is the right to left shunt significantly increased during labor and delivery?

Dr. Whittemore: Yes, particularly if you permit the patient to labor and do the Valsalva maneuver.

Dr. Hur: How would you control this anesthetically?

Dr. Greene: Give them peridural anesthesia and don't allow them to bear down.

Dr. Hook: You cannot control the shunting from the uterus, that is, the emptying of the uterine blood volume during contractions, but you can block the reflex urge to bear down and produce the Valsalva maneuver with conduction anesthesia.

Note: The editors wish to thank Miss Ann Parsons, RN for the preparation of the fetal electrocardiogram tracings.

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Electrocardiogram of the Month: Pseudoarrhythmias

Yale-New Haven Hospital
New Haven, Connecticut

Prepared by
HYMAN M. CHERNOFF, M.D.
Associate Professor of Clinical Medicine,
Yale School of Medicine
Director, Dept. of Electrocardiography
Memorial Unit, Yale-New Haven Hospital

Since the introduction in recent years of newer anti-arrhythmic drugs and electronic devices for the treatment of particular rhythm disorders the ability to recognize specific cardiac arrhythmias has assumed increased significance. However, before embarking on a course of specific treatment it is imperative to rule out pseudoarrhythmia due to recurring artifact.

Below are a number of examples of various types of artifacts that are not infrequently encountered and that have been mistaken by some for true arrhythmias.

A—*Parkinsonian tremor artifact*—the tremor associated with Parkinson's disease often produces deflections in the electrocardiogram that superficially resemble atrial flutter beats in configuration and at rates in the atrial flutter range. Close inspection of the tremor artifact reveals no constant relationship to the ventricular complexes. Since the tremor artifact is usually absent or less pronounced in the chest leads, inspection of these leads will help reveal the true nature of the rhythm that is present.

B—*Hiccough artifact*—deflections due to hiccough may be mistaken for non-conducted atrial premature beats or for non-conducted atrial parasystolic beats or for ventricular parasystolic beats.

C—*Suction pump artifacts*—artifacts produced by a stomach suction tube being operated by a pump while the electrocardiogram is being recorded may be mistaken for non-conducted atrial premature beats, atrial or ventricular parasystolic beats. Similar artifacts may also occur during peritoneal dialysis. The artifact disappears if the pump is turned off.

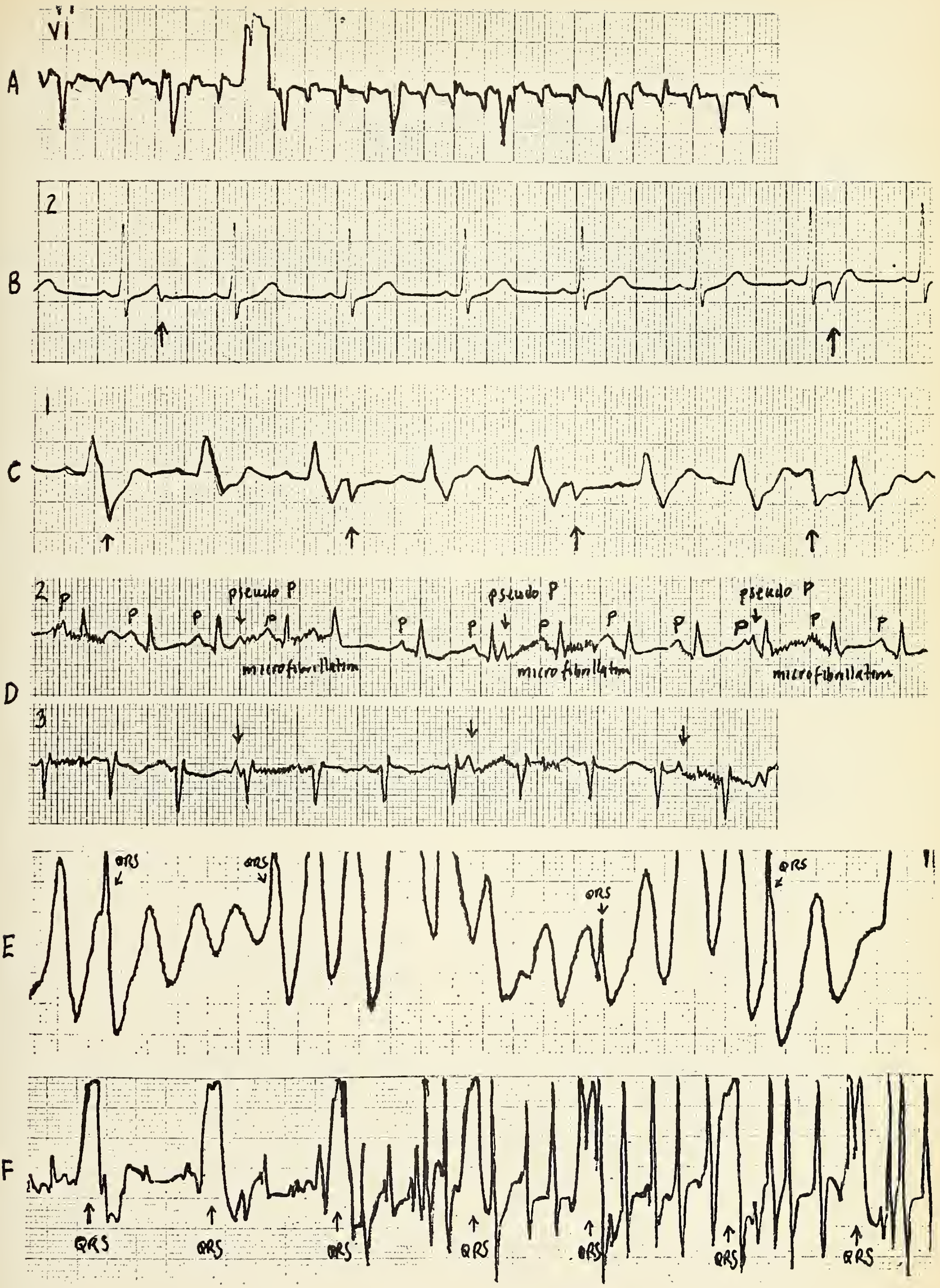
D—*Artifacts arising in the accessory muscles of respiration.*—in patients with severe respiratory distress potentials arising from the accessory muscles of respiration may produce an artifact which consists of an initial deflection (referred to as a pseudo-P wave) followed by a series of small rapid oscillations (referred to as micro-fibrillation). This artifact has been mistakenly interpreted by some as being evidence of atrial dissociation with fibrillation limited to the left atrium.

E—*Artifact from poor electrode contact*—artifacts may occur in chest lead monitoring which have been mistaken for ventricular fibrillation. Close inspection of the tracing reveals the true ventricular complexes in the background. The patient is not pulseless or unconscious as would be the case in the presence of true ventricular fibrillation.

F—*Artifact during convulsions secondary to excess levels of Xylocaine*—the muscle movements during the convulsions may produce rapid recurring deflections which may at first glance be thought to represent ventricular fibrillation. Similar artifacts can occur during shivering.

Pseudo-arrhythmias are caused by artifacts which are superimposed on the deflections of the underlying cardiac rhythm. Accordingly, they bear no constant relationship to the events of the cardiac cycle.

The author wishes to thank Dr. Oscar Roth for supplying tracings E. and F.


A
V1
B
2
C
1
D
2
p
pseudo P
microfibrillation
3
E
QRS
F
QRS

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To the Editor:

A Comment on Town Gown Rivalry

Bert Harte once wrote, "If, of all words of tongue or pen, the saddest are it might have been. More sad are these we daily see: It is but hadn't ought to be."

It is tempting to write about *what is,* and to rehearse how we achieved our present dreary impasse of mutual suspicion and hostility and the growing alienation of those in community practice from the Yale Medical School.

I would rather write of a larger tragedy—The tragedy of what might have been, of lost opportunity.

The city of New Haven and its environs offers a unique opportunity—recognized by many social scientists, for studying on a small scale the problems that confront modern America. Because it is compact and small, accomplishment can be readily ascertained, and one's failures in community endeavor are difficult to conceal. In this microcosm we mirror all the problems that plague our larger cities, including poverty, racial conflict, youthful alienation and ecological crisis.

This is no less true of medical practice. Indeed one of the attractions for practice in this area was the possibility of creating a place for oneself as a recognized member of a smaller, stable community where good medical care was the rule rather than the exception.

Without doubt, the local presence of Yale Medical School and Yale University has in large measure been responsible for the group of highly dedicated, respected and ethically motivated community physicians of high capability in this area.

Similarly, the presence of these physicians has made it possible for the medical school to grow and to evolve to its present position.

Herein lies the roots of our tragedy.

Contrary to expectation, most community physicians are not Philistines awaiting the opportunity to abort the dream. We all recognize that patterns of medical practice are changing and that we must change with them. As a group and as individuals we are flexible and open to innovation and change.

Thus, in the New Haven area, there exists (for how long I do not know,) the opportunity to mount a major cooperative effort to change the face of medical care, research, and education in a community—to demonstrate the viability of private practise *and* group practise; of full time *and* part-time concepts of medical education; of pure research *and* community involvement. With such a union for medical progress—an alliance that combined the best skills of the private *and* full-time physicians; of the hospitals *and* their administrators; *of* the medical school *and* the university; of the local county *and* state medical societies; it would have been possible to demonstrate that these disparate elements could not only live together, but could perhaps even thrive. Then, and only then, could we have done more than pay lip service to community needs, but actually have met them. And yet how far we have moved from this dream.

Warren Bostick first described the full blown form of the "Town Gown Syndrome"

> "In the hemorrhagic form of the sysdrome the assaults become personal, vitriolic and public. Cries come from the medical society opposing medical school expansion, making accusations of waste and charges of medical school physicians "living on the taxpayers." Militant opposing groups appear before elected city officials; the town physicians make an organized refusal to staff the clinical facilities or to refer any patiests to the teaching hospital.
>
> In the full throttle exacerbation institutions are damaged, reputations tarnished, and the medical profession, both in medical school and out, suffers in the public eye. In the heat, the facts at issue are seldom clear or understood by the public and the net result is injury to both parties. . . ."

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In such a conflict there is no victory and compromise is inevitable at a great price in time, money, energy and public esteem. Yet it can happen in New Haven unless we learn to work together in an atmosphere of mutual respect. It can be avoided only if all involved are willing to pay the necessary price.

Most importantly, we must recognize that whatever happens to New Haven Medicine in the next generation will not succeed without the cooperation of community physicians—a necessary ingredient in the equation. With existing population pressures and limited production of physicians there will be need for every able bodied physician to lend a hand. The planners at headquarters need foot soldiers. Where will they come from if not from our ranks? *Secondly,* as experienced and respected physicians dedicated to principles of good medical care, we refuse to allow ourselves to be ignored and treated as archaic remants of a bygone day. In this era, when confrontation is fashionable, we too, insist on our right to participate in the counsels of those who profess the same concern as we do,—achieving the best possible level of medical care for the greatest number. We may disagree about means but our voice must be heard on levels currently closed to us. We need to be involved and doing, not being "done to", and thus, we insist on an equal role in shaping the changes that must come. *Thirdly,* as a group, we currently carry the bulk of medical practise for a large segment of the community—meeting it's everyday needs and problems—indeed rendering care not only to the community at large, but to the families of medical school colleagues and university faculty, and generally, maintaining a level of medical care of high quality. We have little to apologize for, and a great deal to be proud of. We and our patients represent an incalculable asset to the university and the medical school, that must be recognized rather than ignored, respected rather than denigrated.

In turn, we sympathetically recognize that the problems of the medical center are complex and far from solution. The medical school itself is involved in an internal schizophrenic crisis, undecided whether its primary role is in radical innovation in social medicine, or in exploring basic metabolism; in elevating the medical standards of the black community in Africa or in the ghetto; in the field of curriculum revision or in political activism. Until these conflicting roles and priorities are sorted out, our relationship with the medical center will at best, be ambiguous and insecure, subject to the whims of a cut in the federal budget or to even a change in chairmanship of a department.

Ironically, we remain mutually interdependent. No single factor of medical care can exist in a vacuum. Since we are bound together town to gown by geography and by purpose, we had best learn to like one another, even if love is out of the question. But this cannot be a first and second class relationship. At the risk of sounding heretical—I would say that community medical planning is too important to be left to the planners and their client hospital administrators. That would be the tail wagging the dog.

There is need for active utilization of part-time faculty with interest in teaching as well as practice, in association with those full-time clinical colleagues conversant with the problems of medical care, as an important element in planning, policy making and governing the medical center. At the same time, I would hope to see an infusion of full-time faculty members into local and state medical societies on all levels where their opinions could be heard.

Finally, I would welcome a liason body, group or committee, not loaded in advance by a partisan group, but representing the hospitals and the medical school, the medical societies, the group clinics, and the private practitioners, with the power to ascertain the facts in any given planning situation, so as to allay unnecessary fears based on rumor and hearsay, and to anticipate in advance potential areas of disagreement and to deal with them before the fact rather than after them. Such a committee might be empowered to pinpoint specific areas of need in medical care or education and to bring to bear all the forces needed to meet these needs. It would be foolish to feel such a liason committee would end all differences between the various interested parties, for as long as town and gown exists there will be problems and differences. Nevertheless, some degree of understanding is possible and not all our needs are mutually incompatible, particularly if we do not lose sight of our common goal as physicians—the rendering of the best possible medical care while training the best young physicians for the people of America.

Saul S. Milles, M.D., F.A.C.P.

100 York Street
New Haven, Conn. 06511

Library Facilities

To the Editor:

Each Connecticut general hospital has been surveyed three times by the Connecticut Regional Medical Program, with regard to library facilities. The first in 1967 was a mail survey questionnaire conducted by Lee Ash, library consultant of national reputation. I conducted two surveys the first in the late summer, early fall of 1969 and the other just nearing completion in July 1970.

The past two years have seen a dramatic rise in activity in some hospital libraries, and at least a discernible increase in activity in others when measured against minimum rather than ideal or maximum guidelines.

Library services are now available at the Danbury, Greenwich, New Britain and Stamford community hospitals. Other hosiptals are moving toward improving these library services but this needs active support of the physicians on the hospital staffs. For the present an "adequate" library is still the exception in Connecticut's hospitals.

Sincerely yours,
John A. Timour

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One of the greatest reserves of strength that we have in the United States today is the vast number of volunteer women who give of their time and individual ability in all fields of medicine and social work.

Starting with perhaps the first pioneer volunteer, the founder of the American Red Cross, this has grown to unbelieveable proportions. Today every hospital has its own auxiliary dedicated to raising funds for special hospital projects. Last year alone the auxiliary of a large hospital in Hartford furnished three floors of a new dormitory for nurses.

Several years ago the Junior League initiated a pilot course to train women volunteers as social worker aides. This course was presented by a professor from the University of Connecticut School of Social Work and at its completion participants (one of whom was a doctor's wife) were presented with certificates qualifying them to go out doing case work for the Department of Welfare.

In our own auxiliary to the Connecticut Medical Society we, as doctors' wives, have not only started many new projects but have participated in most of the hospital auxiliary programs. Actually the Woman's Auxiliary to the Connecticut Medical Society was formed some twenty-six years ago with the purpose of enhancing the doctor's public image by a program of volunteer service in their individual communities.

A not unimportant facet of this program has been the raising of funds for the purpose of awarding scholarships to medical school students and nurses. One county auxiliary has awarded approximately $60,000.00 in such scholarships. These have been direct grants, not loans. Set up as a Memorial Scholarship Fund a letter of appeal is sent out each year listing the names of physicians who have died during the past year so memorial gifts may be made in their memory.

Many hours have been spent in attending hearings at the Capitol, writing letters, making telephone calls, in general trying to improve the state health laws.

"Meals on Wheels" is a project we participate in every year. This is a service of delivering two meals a day to shut-ins, one hot meal, one cold. Pre-school visual testing and glaucoma detection clinics have also been projects sponsored by the county auxiliaries. A program on Health Careers Education is presented in schools each year. Health information has been made available to the public at county fairs. We have collected medical journals for distribution to medical stations all over the world. One of our latest projects is WASAMA, a program of assistance to medical students or internes in finding a friendly hand, sometimes even housing, in a strange city.

This is a short resume of what we have done in the past. What we must do in the future will depend on what needs to be done. Any state organization is subject to national directives. At present these are: Alcohol, Drug Abuse, Health Careers-Health Manpower, Homemaker Service, Immunization, Mental Health of Children, Sex Education, Smoking, Teenage Veneral Disease, Block Mother Plan, Youth Health and Fitness.

Our main objective as a state auxiliary is to present these national directives to our constituent counties so that they may be used to promote better health in every community in Connecticut.

Since the 1961 White House Conference on Aging, progress has been real. But 20,000,000 older Americans still face many serious problems. Almost one fourth are poor. Nearly all feel a squeeze on their fixed incomes. And with advancing years they must struggle, often in isolation, against multiplying problems in health, housing, employment and their retirement roles and activities.

The same problems also threaten the futures of 42,000,000 middle-aged Americans—more than 18,000,000 men and women, aged 55 to 64, who will be tomorrow's older Americans, and nearly 24,000,000 men and women, aged 45 to 54, who find themselves "old" in the labor market, caught in a conflict between the lengthening of life and the shortening of work careers.

President Nixon has called for a White House Conference on Aging to convene in Washington the week of November 28, 1971, and has asked for the support and assistance of the Woman's Auxiliary to the American Medical Association in making this a successful undertaking. AMA will be serving in a professional capacity. The AMA Committee on Aging has recommended that the Woman's Auxiliary accept President's call for participating to the extent that those interested are willing to accept.

Congress, in authorizing the President to call the second White House Conference on Aging, emphasized a need for developing "recommendations and plans of action" to help middle-aged and older Americans.

The Conference objectives were outlined in Public Law 90-256:

(1) Assuring middle-aged and older persons equal opportunity with others to engage in gainful employment which they are capable of performing; and

(2) Enabling retired persons to enjoy income sufficient for health and for participation in family and community life as self-respecting citizens; and

(3) Providing housing suited to the needs of older persons and at prices they can afford to pay; and

(4) Assisting middle-aged and older persons to make the preparation, develop skills and interests, and find social contacts which will make the gift of added years of life a period of reward and satisfaction; and

(5) Stepping up research designed to relieve old age of its burden of sickness, mental breakdown, and social ostracism; and

(6) Evaluating progress made since the last White House Conference on Aging, and examining the changes which the next decade will bring in the character of the problems confronting older persons . . .

Briefly, the goal is to develop a more realistic and comprehensive national policy for older Americans and to meet what the Conference terms nine priority needs of the elderly: income, health, nutrition, transportation, employment and retirement, education, roles and activities, and spiritual wellbeing.

The names of the state presidents, presidents-elect and chairmen of Home-Centered Health Care Committees (in states where such have been appointed) are being sent to the associate co-ordinator, Mrs. Dorothy Mac Leod. She will forward information and details concerning the role of members of the Woman's Auxiliary in this important project. Let us cooperate on the community level in any way we can.

The National Auxiliary will have two delegates to the Conference itself, and will have an opportunity to recommend two persons to serve on one of the task forces to be organized.—L. V. Gibson

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Doctor's Office

Dr. Henry E. Altenberg announces removal of his office for the practice of child and adult neuropsychiatry from 125 LaSalle Road to 2668 Albany Avenue, West Hartford.

Charles H. Lanzieri, M.D. announces the opening of an office for the practice of obstetrics and gynecology every Thursday, 1 to 4 P.M. at 56 High Street, Thomaston. He also maintains an office at 63 Central Street, Waterbury.

AROUND THE STATE

Dr. Elliot M. Gross was sworn in on September first as the State's first chief medical examiner. Gross, former deputy chief medical examiner in New York City, will head the State's new Office of Medicolegal Investigations. At the swearing-in ceremony were from left Dr. Gross; Dr. Donald R. Hazen, Medical Examiner of Hartford and member of the Medicolegal Commission; Dr. Franklin Foote, Commissioner of the State Department of Health; Dr. Irwin H. Lepow, Chairman of the new Commission on Medicolegal Investigations; and Attorney Arthur H. Schatz, who administered the oath. The appointment of the first chief medical examiner brought to a climax the joint efforts of the CSMS and the Connecticut Bar Association in the sponsoring of legislation which created the new office.

As chief medical examiner, Dr. Elliot M. Gross is temporarily making his headquarters at the University of Connecticut Health Center, McCook Hospital, in Hartford. He also will be a member of the faculty at the University's School of Medicine.

Dr. Gross is a graduate of Columbia College and the New York University School of Medicine. Following completion of his residency in pathology at New York City's Bellevue Hospital, he became a captain in the U.S. Air Force serving as Chief of the Aerospace Pathology Branch at the Armed Forces Institute of Pathology, Washington, D.C.

In August, 1966, he was appointed an associate medical examiner in the Office of the Chief Medical Examiner of the City of New York, remaining in that capacity until May 1. Until September 1, he was an assistant professor of forensic medicine at the New York University School of Medicine and an assistant clinical professor of pathology at the Columbia University, College of Physicians and Surgeons.

Speaking for the new Commission, Chairman Irwin H. Lepow said that Connecticut is extremely fortunate to acquire the services of Dr. Gross:

"He is a well-trained forensic pathologist and one of a handful of men in the country qualified to undertake the task of installing a modern medical investigatory system". Connecticut's present system has been in effect since 1808.

Under the terms of Public Act 699, which was drafted by the Medical-Legal Committee of the State's Bar Association and Connecticut State Medical Society, and passed by the 1969 General Assembly, the Office of Medicolegal Investigations is responsible for carrying out the medical investigation of sudden and suspicious deaths in the state.

Dr. Lepow, who is head of pathology at the University of Connecticut Health Center, went on to say "Perhaps of even greater eventual importance to the general public is the ability of a comprehensive medical examiner program such as this to operate as an early warning system for the detection of potential epidemics and unsuspected diseases".

Dr. John Kriz, assistant professor of pathology at the University-McCook Hospital, has been serving as acting chief medical examiner since the statuatory inception of the office on July 1.

All of the State's present medical examiners have been asked to serve as assistant medical examiners by the Commission. Also, all certified pathologists in community hospitals have been asked to continue conducting post-mortem examinations.

New Haven County

Semi-Annual Report of the Board of Governors New Haven County Medical Association

September 17, 1970

The activities of the Board of Governors of the New Haven County Medical Association have been previously reported in *Connecticut Medicine* each month. Four Board meetings, one leadership seminar with local medical society officers, and six Executive Committee meetings have been held since the annual meeting.

Under the leadership of Past-President Kurt Pelz in 1969 and current President Stewart J. Petrie in 1970, the expanded Executive Committee of the New Haven County Medical Association has evolved a long range program intended to increase the New Haven County Medical Association's involvement with its members and with the public.

The mechanism of getting involved which has been selected has been the use of standing committes and numerous ad hoc committees that have each been carefully charged as to its objectives and obligations by either the Executive Committee or the President. Some of these committees are well along with their projects, a few have finished their tasks and others are just beginning; but all have a definite objective to be attained.

These efforts are being carried out by the largest number of standing and ad hoc committees ever assembled by New Haven County. Additional paid assistants in Public Relations, The Board of Censors and Review Committees, and the county office are helping to do the job.

Areas of involvement include internal and external public relations, peer review, Women's Auxiliary, extensive By-laws revision, "Health Planning", county-wide Emergency and Disaster planning, University-Community physician relations, medical student involvement, implementation of Connecticut State Medical Society programs and objectives, AMA reorganization projects, community health projects, community education, cooperation and communication with local medical societies, integration of provisory members into active committee work, establishment of legislative priorities, and attempts at developing liaison with nonmembers, hospitals, agencies and with numerous non-physician groups who have an interest in health care.

The progress made by the various county committees is reported elsewhere by each committee chairman. The Board of Governors is grateful for the efforts being made by these committees.

At the Annual Connecticut State Medical Society House of Delegates meeting in May 1970 the New Haven County Medical Association was pleased to be co-host with the Connecticut State Medical Society at the libation honoring the installation of Dr. Morris Granoff as President of the Connecticut State Medical Society.

The Executive Committee is most appreciative of the assistance given it in 1970 by Councilors Kurt Pelz, James H. Root, Jr., Jerome K. Freedman, and State President Morris Granoff, State Treasurer Bernard A. Burnham, and State Vice-Speaker of the House Frank Abbott.

Lastly, the Board of Governors of the New Haven County Medical Association has recognized the almost exponential rate at which changes and challenges have accelerated both in medicine and in the community in which we live.

For organized medicine to adapt and effectively deal with this accelerated pace of activities, there is an urgent need for a much greater commitment of manpower and money at the local, county, state and national levels, if physicians are to maintain an effective role in America's medical care system.

Respectfully submitted,
William L. West, M.D., *Clerk*

From the

Connecticut Regional Medical Program

In May CRMP made an award of $15,512 for 1970 to double an existing regional program in gastroenterology involving the Yale-New Haven Medical Center and six community hospitals and to point the way toward a coordinated state-wide educational and patient service system in gastroenterology joining the Yale and University of Connecticut Medical Centers and the 35 general hospitals in the state.

As background, in the April 20, 1967 issue of the *New England Journal of Medicine* Dr. Howard Spiro of Yale and Dr. Vincent DeLuca of Griffin Hospital discussed a joint venture in gastroenterology which was paying dividends in improved patient care and continuing education at Griffin Hospital and was serving to strengthen and extend the graduate education program at Yale.

This joint venture included (1) the appointment of Dr. DeLuca as a member of the clinical faculty in gastroenterology at Yale, (2) the annual joint appointment of a fellow in gastroenterology at Griffin who spent part of his time at Yale, (3) the development of joint conferences and rounds held at Yale and occasionally at Griffin, and (4) the expansion of consultation services by Yale physicians to patients at Griffin and referral of problem cases from Griffin to Yale. The highlight of the article was (5) the evidence presented that the existence of the program—and the presence of the fellow—has had a salutary effect on the whole intellectual atmosphere of the Internal Medicine Department at Griffin Hospital.

In due time, a similar program developed between the Yale Section of Gastroenterology and five other community hospitals; Hartford, St. Raphael's, Bridgeport, St. Vincent's and Norwalk. A working consortium came into being which has proved beneficial to all concerned. The activities of this expanded program are described by Dr. Robert Rosson of Hartford Hospital and Dr. Spiro in the June 8, 1970 issue of *Journal of the American Medical Association.*

Through its May 1970 award CRMP will assist Dr. Spiro and his associates to expand the present program in three significant ways. First, the key program personnel in each of the six existing affiliated hospitals, i.e. the gastroenterologist who serves as program director for the hospital, the fellow and the nurse specialist will seek to determine the gastroenterology needs of patients in nursing homes and other long-term care facilities in their area and chart a course of action to meet those needs. Second, each of the six affiliated hospitals will colonize a program in a nearby community hospital by working with a gastroenterologist designee and a nurse trainee from that hospital. Third, a study will be made of the desirable developments in the field of gastroenterology for the 35 general hospitals of Connecticut and a short and long-range course of action charted.

During the past five years this program has demonstrated the intrinsic value of university-community hospital partnerships in the support of optimum patient care, graduate education, and continuing education of practicing physicians. Building on this sound base, CRMP seeks to demonstrate now that a modest venture involving one university center and six community hospitals can be expanded in 1970 to serve 12 hospitals and a large number of nursing homes and other extended care units. CRMP looks toward a third stage development eventually, in which both university centers, 35 hospitals and 275 nursing homes will be participating in a coordinated venture serving all 3,000,000 people of Connecticut.

The grant from CRMP for 1970 supports three main functions. First, there are part-time salaries for a medical coordinator for the over-all program (whose duties are largely administrative), his administrative assistant and a sociologist-evaluator for the program. Second, there is the full-time salary of an Associate Program Director who has major responsiblity for staging the teaching conferences at Yale and for conducting teaching rounds at the affiliated hospitals on a regular basis. Third, modest consultation fees are provided to cover the time spent by the program directors and others in the community hospitals during their field activities.

The fact is that most of the costs of this total program are covered by funds from Connecticut sources. Dr. Howard Spiro, the founder and moving spirit of the program, is paid entirely by Yale

University. The basic costs of the program in each of the six affiliated community hospitals are being paid by those hospitals at an estimated level of $21,000 per hospital for 1970. For 1971 it is anticipated that there will be considerable assumption of 1970 CRMP financing by the local hospitals and further assistance through the recently organized Connecticut Digestive Disease Foundation.

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Science News

Another Herbicide On The Black List

(*Nature*, 226, 309, April 25, 1970) Herbicidal chickens from Vietnam came home to roost last week when D. M. Jacqueline Verrett of the FDA showed off to the Chairman of a Congressional Committee, two trays of deformed chicks born of eggs dosed with the controversial herbicide 2.4.5-T.

Accordingly the Secretary of Agriculture, the Interior and HEW decided to restrict the use of 2.4.5-T in circumstances where foodstuffs for human consumption might be contaminated.

During the past 6 years groups of scientists have campaigned against 2.4.5-T on two separate counts. This herbicide has been widely used in Vietnam as a defoliant and the AAAS has drawn attention to the long term ecological hazards of the practice.

Now there is concern about the potential teratogenic effects of this herbicide. The Department of Defense has now asked those responsible for defoliation in Vietnam to pay heed to the findings which have now come to light. However, "paying heed" is not the same as banning it.—L.H.N.

Cigarette Ads

(*Science*: 168, 804, May 15, 1970) The President has signed a bill banning cigarette advertising on radio and television after next January 1, 1971.

The cutoff date will permit cigarette advertising on the telecasts of football games on New Year's Day.

The bill also prescribes a stronger warning lable for cigarette packages and gives the Federal Trade Commission authority to require a health warning in other advertisements after July 1, 1971, provided Congress has been notified 6 months in advance.—L.H.N.

Clinical Significance Of Hyperuricemia In Routinely Screened Hospitalized Men

(*JAMA*: 211, 277, 1970, Paulus, H. E., Coutts, A., Calabro, J. J., Klinenberg, J. R.) Serum urate values greates than 7 mg/100 ml were found in 13.2% of 4,148 male patients screened at a hospital. When 200 patients with hyperuricemia were studied in detail, the most common causes of urate elevation were azotemia 20 per cent, acidosis 20 per cent and ingestion of diuretics 20 per cent. Only 12% had a history of gout.

Eighty per cent (160 patients) did not require specific therapy, the remaining 20% either had gout or had sustained hyperuricemia (values above 9 mg/100 ml) which warranted drug treatment.

These findings suggest that abnormal data generated by a routine laboratory screening program do not confirm a diagnosis or justify therapy, but merely represent a different type of "chief complaint" which must be carefully investigated before a diagnosis is made or therapy considered.—L.H.N.

Marihuana And Temporal Distengration

(*Science*, 168, 1118, May 29, 1970, Melges, F. T., et al.) High oral doses of marihuana extract calibrated for content of tetrahydrocannabinol, significantly impaired the serial coordination of cognitive operations during a task that required sequential adjustments in reaching a goal. This disintegration of sequential thought is related to impaired immediate memory.

Serial immediate memory errors include loss of place, failure to alternate between subtraction and addition and blocking.

Lack of goal-directedness and loose associations were common in the speech patterns of the subjects when they were under the influence of the drug.—L.H.N.

Malaria Resistance: Artificial Induction With A Partially Purified Plasmodial Fraction

(*Science*. 168: 1117, May 29, 1970, D'Antonio, L. E., et al.) The isolation of specific host-free, plasmodial fractions effective in the induction of artificial resistance to malaria has never been reported before. Such substances are crucial in advancing immunochemistry, immunobiology, and vaccine technology of malaria and related diseases.

Plasmodia were released from mouse erythrocytes by passage through a French pressure cell. The released organisms were washed and disintegrated. A soluble portion contained an erythrocyte-free plasmodial fraction which behaved as a vaccine, preventing parasitemia, anemia and death in mice subsequently challenged with living Plasmodia berghei.—L.H.N.

Sexual Activity and the Postcoronary Care Patient

(*Medical Aspects Human Sex. 3,* 70, 1969, Hellerstein, H. K., Friedman, E. H.) A study was made of sexual activity of 91 middle-aged middle class men, 48 with ASHD and 43 normal, but coronary prone.

In over half of the ASHD sexual activity decreased with age and decreased further after development of a myocardial infarct.

Symptoms of coronary insufficiency infrequently influenced return to sexual activity. As physical fitness increased so did sexual activity.

A basis for counseling recognizes both physical and psychologic factors. A physiologic measure of the adequacy the advice may be obtained by a "sexexercise" tolerance test.—L.H.N.

Chest Pain Coronary Artery Disease and Coronary Cinearteriography

(*Chest.* 57, 41, 1970, Leon H. F., et al.) Patients with a typical chest pain and a normal response to exercise will invariably show normally patent vessels while patients with typical angina and an abnormal ECG response to exercise will show major obstructive disease usually of more than 2 major vessels.

Coronary arteriography is pertinent in those patients with either atypical chest pain and an abnormal response to exercise, or typical chest pain and a normal response to exercise.

Selective coronary visualization is imperative in patients being considered for revascularization procedures.—L.H.N.

Newspaper Pollution

(*Nature.* 227, 12, July 4, 1970) The National Science Foundation has awarded $53,000 to two graduate students at the School of Medicine at Stanford University to determine the effectiveness with which the news media around San Francisco Bay handle information about pollution of the environment.

Mr. David Sachs and Jan Krupp will first survey the places and the causes of environmental pollution. They will then survey the treatment of these questions by the news media which operate in this region. The team will then determine how accurately and fully the problems of the environment are dealt with in the news media.

They hope to turn up a number of news stories so far neglected by the journalists. The idea also is for the study to provide the mass media on how best to cover environmental deterioration and also on the best way "to interpret science and government reports on environmental problems".—L.H.N.

New Institute of Medicine

(*Nature.* 227, 12, July 4, 1970) The National Academy of Sciences (NAS) will set up an Institute of Medicine. It will eventually have members serving for fixed terms. The new body will provide advice on medical matters. Looking ahead are the problems which will be created by the setting up of a National Health Service now on the horizon.

The old Board of NAS won its spurs with a public statement on the ethics of heart transplants. More recently the board has been worrying about the reform of medical education and the cases of unrest in medical schools.

The New Institute will consist of Medical people, lawyers, and administrators. The organization already includes Professor Adam Yarmolinsky, a Harvard Lawyer. The Chairman of the New Institute will be the present chairman of the board, Professor Walsh McDermott of Cornell University Medical School.

Members of the NAS are concerned that the diversity of interests of the likely members will not fit easily into the traditional concept of a learned academy.–L.H.N.

Hanford Biology Symposium

(*Nature.* 226, 1090, June 20, 1970) The annual Hanford Biology Symposium was held at Richland, Washington, June 2-5, 1970. A notable feature of the meeting was an attempt to define effects of pollutants not only in terms of pulmonary, structural, and functional changes affecting gas exchange, but also in terms of underlying biochemistry.

Several pollutants have been found to affect the capacity of alveolar microphage to kill organisms this being the principal mechanism by which the lung resists bacterial infection. Some of the most striking effects are produced by particulate pollutants such as silica and asbestos.

Of the gaseous pollutants most work so far has been carried out with oxidizing atmospheres such as high oxygen ozone and nitrogen dioxide. These oxidize lipids and produce marked changes in lung structure and function. The structural changes included degeneration of endothelial and type I alveolar epithelial cells.—L.H.N.

MEETING NOTICES

The information on this "notices" page is offered as a service to all specialty groups and allied health agencies in order to publicize postgraduate educational opportunities available to subscribers. The deadline for publication in Connecticut Medicine is the tenth of the preceding month, i.e., the tenth of September for the October issue. Send copy to: Connecticut State Medical Society, 160 St. Ronan Street, New Haven, Connecticut 06511.

GENERAL

November 19—Thursday
Connecticut State Medical Society
Semi-Annual Meeting of the House of Delegates
Hartford Hilton Hotel, Hartford, Connecticut
April 27-29—Tuesday-Thursday
Connecticut State Medical Society
179th Annual Meeting of the Connecticut State Medical Society
Hartford Hilton Hotel, Hartford, Connecticut

GENERAL MEDICINE

November 11-14—Wednesday-Saturday
4th Annual Postgraduate Seminar
Tides Hotel, Redington Beach, Florida
"Today's Hospital Problems: An Interdisciplinary Approach"
Designed for Chiefs of Staff, Hospital Directors and Governing Personnel.
Contact: University of Florida, Miller Health Center, Gainesville, Florida.
November 15-19—Sunday-Thursday
17th Annual Meeting of the Academy of Psychosomatic Medicine
Princess Hotel, Hamilton, Bermuda
Theme for the sixty presentations: "Treating Emotional Illness"
Contact: Edwin Dunlop, M.D., 150 Emory Street, Attleboro, Massachustts, 02703 (617-222-2600).

INTERNAL MEDICINE AND SURGERY

September 15-June 1—Tuesdays
Lecture Series on Medical Emergencies
Lawrence and Memorial Hospitals, New London, Connecticut
Contact: Edward Gipstein, M.D., Director of Medical Education. (442-0711 ext. 361).
October 26-28—Monday-Wednesday
An American College of Physicians Course: "New Concepts in Basic and Applied Hematology"
Jefferson Medical College, Philadelphia, Penna.
Contact: A.C.P., 4200 Pine Street, Philadelphia, Penna. 19104.
November 11—Wednesday 1:30 P.M.-4:45 P.M.
"Oral Hypoglycemic Agents in the Treatment of Diabetes Mellitus"
Fitkin Amphitheatre, Yale-New Haven Medical Center
Speakers: Philip Felig, M.D., Yale University School of Medicine; Henry T. Ricketts, M.D., University of Chicago's Pritzker School of Medicine; Max Miller, M.D., Case-Western Reserve University School of Medicine; Alexander Marble, M.D., Harvard Medical School.
Contact: Yale University, Department of Internal Medicine, New Haven (436-0139).
November 11-13—Wednesday-Friday
An American College of Physicians Course: "Genetics for the Internist"
New York Hospital-Cornell Medical Center, New York City
Contact: A.C.P., 4200 Pine Street, Philadelphia, Penna.
January 14, 1971—Thursday
Annual Meeting of the Connecticut Chapter American College of Surgeons
Hotel Sonesta, Hartford, Connecticut

OPHTHALMOLOGY

October 30—Friday
All Day Meeting: Ocular Trauma
Yale University School of Medicine
Topics: Orbits and Lids, Cornea and Chemical Injuries, Intraocular Foreign Bodies, Intraocular Surgery, Infection and Sympathetic Ophthalmia, Pathology
Sponsored by the Connecticut State Medical Society, the Section on Ophthalmology and the Yale University School of Medicine
$13.00 covers luncheon at the Medical School and dinner at the Park Plaza
Contact: Frederick D. Williams, M.D., 1 Atlantic Street, Stamford, Connecticut

PEDIATRIC

November 12—Thursday

Annual Pediatrics Symposium: "The Clinical Application of Genetics"

St. Francis Hospital, Hartford, Connecticut

Speakers: Panel of physicians form the Albert Einstein College of Medicine under the direction of Harold M. Nitowsky, M.D.

Contact: William E. Hart, M.D., Director of Pediatrics (249-8281).

November 18—Wednesday

Perinatal Seminar

Harkness Auditorium, Yale-New Haven Medical Center

Speakers will include: Dr. Alex Minkowski, Director of the Centre de Recherches Biologiques Neonatales, Paris, France. Two discussions: "The Biochemistry of the Small for Dates Infant," "The Pediatrician and the Problem of High Risk Pregnancies".

Richard Banfield, M.D., and Ruth Wilf, Ph.D.: Discussion on various aspects of a prepared child birth program.

Mr. Samuel Shapiro, Director of Research and Statistics for the Health Insurance Plan of Greater New York, "Abortion Practices as They Relate to Perinatal Morbidity and Mortality."

Panel Discussion on Neonatal Intensive Care and Transitional Care of the New Born Infant:

Moderator: Robert H. Usher, M.D., Neonatal Unit and Royal Victoria Hospital, Montreal, Quebec, Canada.

Alexander Campbell, M.D., Associate Professor of Pediatrics and Director of the Neonatal Unit at Yale University School of Medicine.

Stanley James, M.D., Columbia University College of Medicine.

Jeryl Gagliardi, R.N., New Born Intensive Care Unit, Yale-New Haven Hospital.

Contact: Robert L. Harris, M.D., 581 Farmington Avenue, Hartford, Connecticut. (Telephone 203-232-5202).

December 9-12—Wednesday-Saturday

Pediatric—Cardiology Postgraduate Course

Happy Dolphin Inn, St. Petersbury Beach, Florida

"Congenitial and Acquired Heart Disease in Infants and Children"

Contact: Gerald Hughes, M.D., American Academy of Pediatrics, Box 1034, Evanston, Illinois 60204.

PSYCHIATRY

November 3, 10 and 24—Tuesdays 10:30 A.M.

Lecture Series

Connecticut Valley Hospital, Middletown, Connecticut

Speaker: Jules V. Coleman, M.D.

November 3: "Personality Development and Psychopathology: The Problem of Psychiatric Nomenclature in Relation to Epidemiology"

November 10: "The Social—Ecologic Role of Psychiatric Treatment"

November 24: "The Distribution of Mental Disorders in Populations: Challenges of Psychiatric Epidemiology"

SCHOOL HEALTH

October 30—Friday 8:30 A.M.-3:30 P.M.

Slade Jr. High School, New Britain, Connecticut

Speaker: Miss Gertrude Cherescavich, Associate Professor and Director of Nursing Service, New York University. "The School Nurse Makes A Difference in Adolescent Living"

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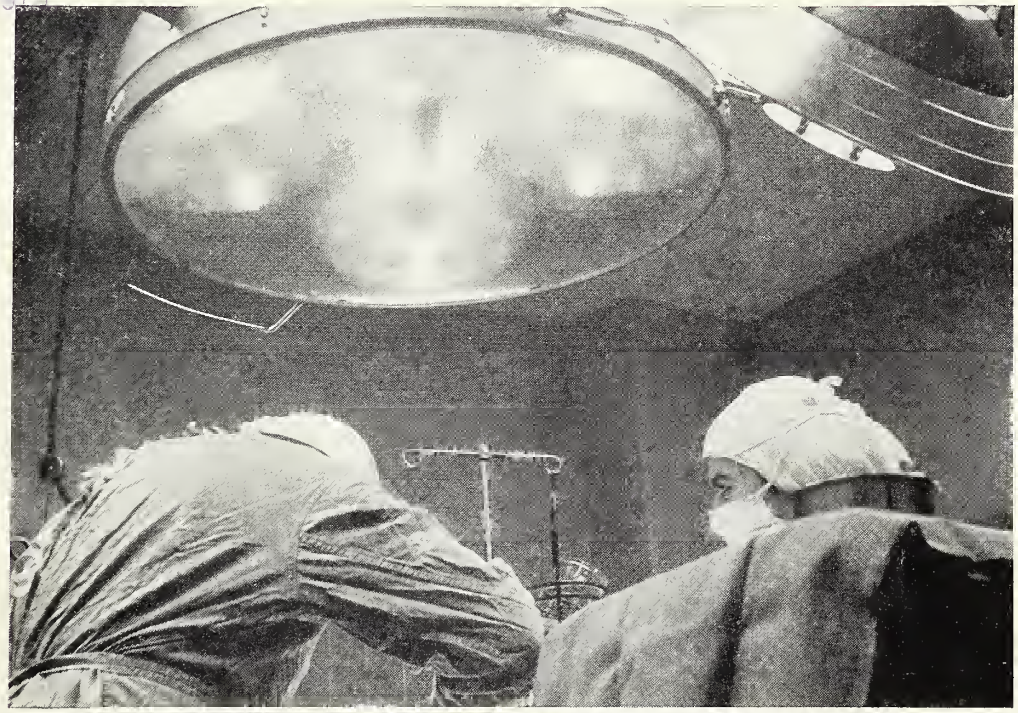
SYMPOSIUM ON SURGICAL PAPERS: James H. Foster, M.D., *Guest Editor*



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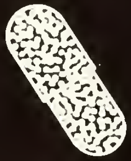

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CONTENTS

editorials

Movements Of The Human Fetus During Gestation . . . 757
The Biology Of Alcoholism . . . 757
Diagnostic Progress In Cancer Tests . . . 759
Drug Abuse Overtaking Alcoholism As A Business Problem 763
Methods For Pest Control In Agriculture . . . 765
Marihuana: I . . . 766
Problems And Hazards Of Pesticides . . . 768
Water Pollution Abatement . . . 772
Environmental Causes Of Congenital Defects . . . 776
How Much Superstition In Our College Students . . . 777
Peer Evaluation Of The Office Laboratory . . . 778

scientific

Foreword, *James H. Foster, M.D., Guest Editor* . . . 782
Operative Management Of Esophageal Atresia By End-To-Side Anastomosis And Ligation Of The Tracheo-Esophageal Fistula, *Robert J. Touloukian, M.D. and Lawrence K. Pickett, M.D.* . . . 783
An Experience With Pre-Scalene Lymph Node Biopsy And Mediastinoscopy, *Joseph P. Dineen, M.D. and Jashwant Patel, M.D.* . . . 789
Current Controversies Surrounding Major Hepatic Resections, *Gerald O. Strauch, M.D.* . . . 792
Femoral-Tibial Bypass: Salvage Of Ischemic Lower Extremities With Inadequate Popliteal Runoff, *John E. Fenn, M.D. and Donald B. Alderman, M.D.* . . . 796
Misplaced Central Venous Pressure Catheters, *Robert T. Schweizer, M.D. and James H. Foster, M.D.* . . . 802
The Zinc Story: An Introduction, *Donald F. Bradley, Jr., M.D.* 805
Present Status Of Augmentation Mammaplasty, *Tibor de Cholnoky, M.D.* . . . 808
Transduodenal Sphincterotomy And Choledocholithiasis, *William A. Whalen, M.D. and James W. Major, M.D.* . 810

departments

The President's Page . . . 812
From The Executive Director's Office . . . 814
Physician's Placement Service . . . 817
Law-Medicine Notes, *J. Alfred Fabro, M.D.* . . . 819
X-Ray Of The Month, *Arnold B. Rilance, M.D.* . . . 822
Electrocardiogram-Of-The Month, *Hyman M. Chernoff, M.D.* 824
Woman's Auxiliary . . . 828

miscellaneous

Doctor's Office . . . 820
Welcome New Members . . . 820
Obituaries:
    Louis Antupit, M.D. . . . 826
    Robert R. Nesbit, M.D. . . . 826
In Memoriam . . . 827
Connecticut Regional Medical Program . . . 829
Around The State . . . 830
Science News . . . 831
Meeting Notices . . . 835

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Movements Of The Human Fetus During Gestation

The development of prenatal behavior has not been adequately described for either the normal or defective fetus largely because adequate techniques for recording fetal behavior have been lacking. Typically fetal development has been evaluated from the mother's report of fetal activity. It is difficult to summarize findings from such records because of great variability in recording methods used and period of gestation recorded. Now Edwards and Edwards have devised a method for continuously recording fetal movements during normal activities of the mother and during laboratory visits. With this method, they have been able to determine the time course of changes in fetal movement which is a measure of behavioral development in the human fetus.

Fetal movements appear to develop in three stages. In the early stage, rates of movement generally vary between 0 and 1 or 1.5 movements per 100 minutes. Then the rate accelerates and is maintained between 2 and 10 per 10 minutes until the fetus changes position. The rates then become more variable and decrease until birth. All eight of their patients showed the same general pattern despite variations in absolute rates.

Fetal activity occurs as discrete movements, bursts of activity, and prolonged activity. Four records were taken while the woman worked at her desk. Another, taken during a social activity when the woman ingested some alcohol. is characterized by prolonged fetal movement. The authors' method of recording reflects patterns of movement and changes in the frequency of movements. Bursts of activity and prolonged activity have not been previously described. Previously different types of fetal movements or the percentage of time when the fetus was active have been recorded during the last few months of pregnancy.

Between two and four different types of movements such as kicks, squirms, ripples, and hiccups or quickening movements, slow movements, and rhythmic movements were reported. Edwards has focused on the record of activity rather than on the type of movement, and it is not clear how these earlier records compare with theirs. Furthermore, Edwards compared rates of fetal movement recorded automatically with the 4-hour samples and daily rates, since most previous studies used samples taken over a short time.

In all cases, samples ranging from 30-200 minutes were not representative of the daily rates. Accordingly the 4-hour rates were found closest to the daily rates. There did not appear to be systematic relationships between the mother's activity and changes in daily rates, 4-hour rates or automatically recorded rates of fetal movement.

The similarity in behavior of all fetuses is evidence that a direct and continuous account of fetal development is possible by Edwards' method.—L.H.N.

Reference

1. Edwards, D.DeA. Edwards, J. S. Fetal Movement: Development and Time Course, *Science* 169: 95, July 3, 1970.

The Biology Of Alcoholism

Until recently, most alcohol-related problems were perceived as a moral issue. Current motivation for alcohol related research derives from its major public health problems that seriously affect both the quality and the length of life for over 8 million Americans. Since serious intercurrent illness is so prevalent in persons with alcohol-related problems, a major concern of physicians and biomedical scientists during the past decade has been the diagnosis and treatment of nutritional, infectious, toxic and metabolic disorders associated with alcoholism. The disorders of organ function such as the liver, heart and brain in alcoholics and heavy drinkers are well described in the literature. Mendelson now examines the aspects of alcohol metabolism and the biological concomitants of excessive alcohol use that may contribute to our understanding of the natural history of alcohol addiction.

The pharmacologic criteria for alcohol addiction are essentially the same as those employed for a variety of other addictive disorders, namely tolerance and physical dependence. Two possible factors have been postulated in tolerance: an enhanced rate of degradation of ethanol termed metabolic tolerance; and increased degree of cellular adaptation to ethanol in the central nervous system.

The first major step in oxidation of ethanol is to acetaldehyde which is then converted to acetyl CO-enzyme A. Regardless of how much alcohol a patient takes, his acetaldehyde remains low and relatively constant. This makes it unlikely that acetaldehyde plays a role in the process of alcohol tolerance and leaves the major addictive agent in alcoholism to ethanol itself and not its initial metabolite. Thus if a drinker develops tolerance to ethanol it must mean that he metabolizes it more quickly and his nervous system also develops tolerance to it.

Presently two methods exist to enhance ethanol metabolism. One is the use of fructose but its application to treatment of acute ethanol intoxication has not yet occurred. Perhaps the most important factor enhancing rate of ethanol metabolism in man is dietary intake. Well fed rats, for example, show twice the rate of alcohol metabolism as do fasted rats. Mendelson showed a progressive increase in blood alcohol levels as caloric intake was reduced in human subjects. It is well known that alcoholics tend to eat poorly while they are drinking and nutritional derangements in these patients are a common clinical phenomenon. Mendelson raises the question whether the drinkers refraining from food is not really an effort on his part to achieve a greater behavorial response.

At present there are strong data to support the view that tolerance for ethanol by alcoholics is related to factors that regulate the metabolism of ethanol. Enhanced rate of metabolism occurs in man after prolonged drinking. However, this enhanced metabolic rate cannot explain the considerable degree of tolerance for alcohol shown by alcoholics who may have very high blood levels and nevertheless continue to perform cognitive and perceptual motor tasks reasonably well. It must mean that in addition to metabolic rate there is also central nervous system cellular adaptation to ethanol.

Adaptation does occur in systems ranging from autonomous single cell units to complex organ function. There is some evidence that tolerance to ethanol may be associated with decreased release of acetyl-choline. Another idea is that active ion transport in the nervous system may be suppressed by relatively low ethanol concentrations.[2] There is as yet no firm explanation for the mechanism of tolerance developed by the central nervous system and much work is needed in this area.

Dependence is the second major pharmacologic criterion of alcohol addiction. Evidence of this dependence is the occurrence of withdrawal signs and symptoms such as salivation, nausea, vomiting and epileptiform seizures. Formerly, it was thought that the withdrawal syndrome reflected intercurrent illness or vitamin and nutritional deficiency rather than the effects of cessation of drinking. Now it is clear withdrawal symptoms occur as a result of cessation of drinking and cannot be accounted for by associated nutritional deficiency. It has been suggested that chronic central nervous system depression by drugs such as morphine, barbiturates, and alcohol is tantamount to disuse. Upon removal of the drugs there is a rebound hyperexcitability of the functional systems depressed. Accordingly, drugs that elevate thresholds for chemically induced seizures would be expected to exhibit lower seizure thresholds during withdrawal. Besides effects on the central nervous system there are endocrine alternatives also such as increased cortisol levels in the blood and also increased aldosterone secretion.

It is probable that both tolerance to and physical dependence on alcohol have multiple determinants that involve a complex interaction of increased endocrine and metabolic factors and neural factors. Alcohol addiction is thus seen to be characterized by processes of tolerance and dependence, the mechanics of which are poorly understood.

At present there is no compelling evidence that tolerance is associated with inherent or adaptive changes in ethanol metabolism in alcoholics. Physical dependence and tolerance are probably due to modification in the central nervous system that in turn are affected by peripheral endocrine and metabolic concomitants of chronic ethanol intake. Elucidation of this process requires development of an animal model that fulfills the physiologic and behavioral criteria of addiction to alcohol in man. It now seems that the rat might be the correct animal model.

Cultural and social factors certainly contribute to the genesis and natural history of alcoholism. However successful, intervention for both the primary disorder and associated illnesses appears to require a better understanding of the biologic factors that underlie the addictive state.—L.H.N.

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Diagnostic Progress In Cancer Tests

Reports dealing with the immunology of cancer—and its possible diagnostic and therapeutic applications—made up a large part of the programs of two recent major conferences, the Tenth International Cancer Congress in Houston and the American Association for Cancer Research (AACR) meeting in Philadelphia.

Fetal antigens have been associated with specific types of tumors in later life and the diagnostic tests are entering widespread use. Preliminary diagnoses of tumors of the digestive tract, liver, and pancreas can be made by detecting fetal antigens in the blood stream, said Dr. Phil Gold of McGill University. These protein-polysaccharides are found in the digestive organs of the human embryo and fetus, but only during the first two trimesters of gestation. When the carcinoembryonic antigens (CEA) appear later in life, they represent a "tumor-specific constituent of all adenocarcinomas arising from the endodermally-derived digestive system epithelium."

A radioassay capable of detecting the CEA in as little as one-billionth part per milliliter of serum promises to be an accurate screening test for cancers of the bowel. Patients who have the antigen in their blood can then be given barium roentgenograms or other diagnostic examinations.

In France a different set of fetal antigens is already being applied clinically in an immunodiffusion test to detect hepatomas and malignant teratoblastomas. Thus the patients who have primary liver cancer have in the serum samples alpha-fetoproteins. However, histologically confirmed hepatocellular carcinomas can develop without secretion of alpha-fetoprotein. However, if found, this fetal antigen represents existence of liver malignancy.

This discovery of still another fetal antigen system unrelated to the previous ones and associated with a wide variety of human tumors was reported by Dr. Eugene M. Edynak and his coworkers. They tested many sera and tissue extracts against serum from a patient with medullary carcinoma of the breast. What they call a "gamma fetal protein" was precipitated out in 70% of 116 malignant neoplasms, from such organ systems as the breasts, colon, lung and ovary. Sixteen of 20 extracts of benign tumors such as fibroadenomata, also contained the gamma fetal protein.

The antigen was not found in over 100 normal tissue specimens, and occurred in only two of 65 diseased but non-malignant tissue specimens. The antigen and antibody detectable in the sera of some cancer patients could not be found in the sera of 111 normal persons and 129 patients with hepatitis or infectious mononucleosis.

Although immunologic methods for diagnosing and studying these specific types of cancer appear to be gaining acceptance, the future of immunotherapy for malignant neoplasms seems less certain. Several claims of clinical success, however, were made. Dr. Philippine Hartmann, a gynecologist in private practice in Munich reported that she induced regressions and even some remissions in 7 of 12 patients treated for "incurable cancers" of the ovaries, uterus, or breast. Two of 4 cases with complete regressions were tumor-free four years after treatment. She removed as much of each primary tumor as possible and cultured the cancer cells with fetal tissue to accomplish "potentiation" of the tumor antigen. Despite extensive metastases and far advanced cachexia, definite cytolysis of the tumors could be achieved with the washed cell sediment of these cultures.

Georges Mathe claimed he had produced remissions lasting up to five years in 7 of 20 patients suffering from acute lymphocytic leukemia. The ten controls on chemotherapeutic regimen relapsed after about four months. In the hope of enhancing the patients immunological response, Dr. D. M. Mumford of Baylor used Corynebacterium parvum in treating patients with stage IV melanoma. One patient is still in remission after 26 months. Others used phytohemagglutinin to boost the cytotoxic strength of lymphocytes in vitro. This method was also used by Stanford physicians in patients with pulmonary metastases with 50 per cent reduction in the size of pulmonary metastases in three of five cancer patients said Dr. John H. Frenster.

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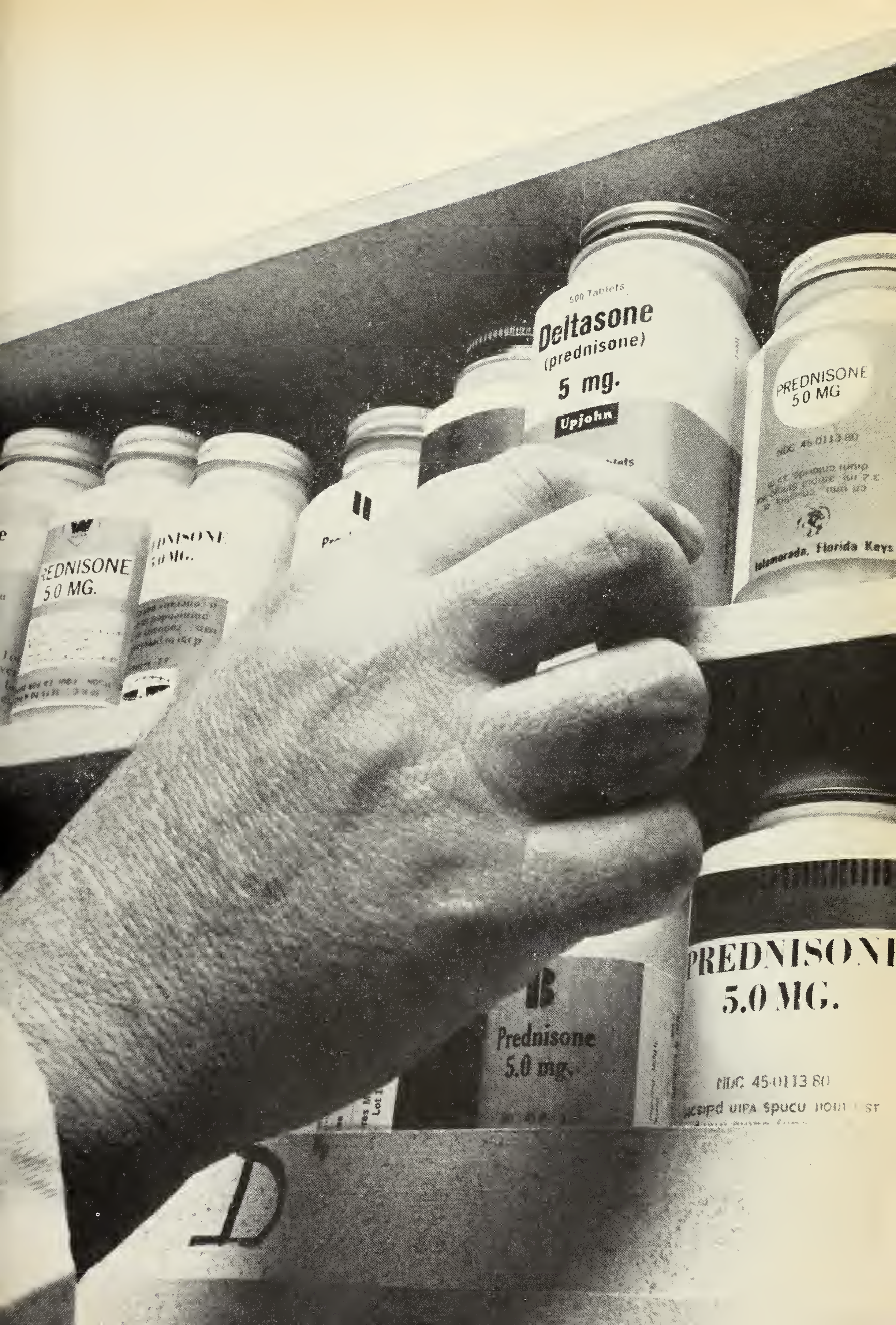
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Contraindications: As for all other corticoids. *Considered Absolute*—herpes simplex keratitis, acute psychoses and latent, healed or active tuberculosis. May be lifesaving in certain cases of pulmonary or meningeal tuberculosis, but should be used only in conjunction with adequate and effective antituberculous therapy to which causative organisms are shown to be sensitive. *Considered Relative*—active or latent peptic ulcer, Cushing's syndrome, diverticulitis, fresh intestinal anastomoses, osteoporosis, renal insufficiency, thromboembolic tendencies, psychotic tendencies, diabetes mellitus, hypertension, local or systemic infections including vaccinia, varicella and other exanthematous diseases, and fungal infections, and, pregnancy particularly during the first trimester because of observation of fetal anomalies in experimental animals. If necessary to give corticosteroids during pregnancy, watch newborn infants closely for signs of hypoadrenalism and institute appropriate therapy if signs appear.

If corticoids are used in the above conditions, weigh risks against benefits.

Precautions: Deltasone should be given only with full knowledge of characteristic activity of and varied responses to corticoids. Because of inhibiting effect on fibroplasia, corticoids may mask signs of and enhance spread of infection; hence, watch patients closely, and if intercurrent infection occurs, control with appropriate antibacterial measures. If possible, avoid abrupt cessation of corticosteroid therapy because of the danger of superimposing adrenocorticoid insufficiency on the infectious process. Prolonged hormone therapy usually causes a reduction in the activity and size of the adrenal cortex. When discontinuing therapy, relative adrenocortical insufficiency may be avoided by gradual reduction of dose. However, a potentially critical degree of insufficiency may persist asymptomatically for some time even after gradual discontinuation of adrenocortical steroids. Therefore, if a patient is subjected to significant stress, such as surgery, trauma, or severe illness while being treated, or within one year (occasionally up to two years) after treatment has been terminated, hormone therapy should be augmented or reinstituted and continued for the duration of the stress and immediately following it. Since mineralocorticoid secretion may be impaired, salt and/or desoxycorticosterone should be administered conjunctively. It is preferable to use a soluble hormone preparation in the immediate preoperative and postoperative periods.

Although unlikely with Deltasone, average and large doses of corticosteroids can cause elevation of blood pressure, salt and water retention and increased potassium and calcium excretion. Dietary salt restriction and potassium supplementation may be necessary. Glucocorticoid steroids may aggravate diabetes mellitus so that higher insulin dosage may become necessary or manifestations of latent diabetes mellitus may be precipitated. Corticosteroids may aggravate myasthenic symptoms in myasthenia gravis and should be given with proper precautions.

Muscle weakness, in some instances, attributed to hypopotassemia, has been reported following prolonged systemically administered corticoids. Excessive potassium loss, like excessive sodium retention, is not likely to be induced with effective maintenance doses of Deltasone (prednisone), however, keep this effect in mind and perform periodic serum potassium determinations in patients on prolonged corticoid therapy. Muscle weakness occurring with normal serum potassium levels may be due to disturbance in muscle metabolism. Severe myopathy is associated with substantial doses of steroids for prolonged periods, and evidence indicates it occurs more frequently with 9-alpha-fluro steroids. Replacement with non-fluorinated steroid has, in some instances, resulted in improvement.

Retardation of linear growth, roughly proportional to dose, has been noted in children on corticoids for six months or more. Following cessation of therapy, growth rate may be accelerated. Therefore, carefully observe growth of children on prolonged corticoid and if growth is retarded, reduce dose sufficiently to permit recovery before epiphyseal closure. Make every effort to avoid corticoids during pregnancy, since spontaneous remission of some diseases such as rheumatoid arthritis may occur. Long term corticoid therapy may evoke hyperacidity or peptic ulcer, therefore, as prophylaxis, an ulcer regimen and antacid are highly recommended. Take X-rays in peptic ulcer patients complaining of gastric distress, and, whether or not changes are noted, an ulcer regimen is recommended. Since prednisone causes less salt and water retention than many other glucocorticoids, patients should be observed closely for development of undesirable hormonal effects that are less obvious indications of steroid toxicity than edema and hypertension due to salt and water retention. Continued supervision of patients after cessation of therapy is essential, since there may be a sudden reappearance of severe disease manifestation.

Adverse Reactions: Adverse reactions associated with use of corticoids include: Cushing's syndrome, moon facies, supraclavicular fat pads, hirsutism, striae and acne; relative adrenocortical insufficiency particularly in time of stress due to trauma, surgery or severe illness; protein catabolism with negative nitrogen balance; electrolyte imbalance; alteration of glucose metabolism with aggravation of diabetes mellitus including hyperglycemia and glycosuria; osteoporosis reversible only with difficulty; spontaneous fractures; aseptic necrosis of the hip and humerus; activation and complication of peptic ulcer including perforation and hemorrhage; aggravation or masking of infection; increased blood pressure; convulsions; petechiae and purpura; menstrual irregularities including amenorrhea, spotting or prolonged bleeding; insomnia; psychic disturbances especially abnormal euphoria; nervousness; posterior subcapsular cataracts occasionally requiring extraction; increased intraocular tension; increased intracranial pressure with papilledema (pseudotumor cerebri); pancreatitis; necrotizing angiitis; thinning of scalp hair; suppression of growth in children; thromboembolic complications; facial erythema; allergic skin reactions; ulcerative esophagitis; sweating; vertigo; weakness; myopathy; headache; exophthalmos. Adverse reactions are usually reversible and usually disappear when drug is discontinued.

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In addition to hearing of some clinical successes, the scientists at the Cancer Congress also heard papers describing immunotherapeutic failure. For example, after recounting his own failures, Dr. Chester M. Southam concluded, "Immunotherapy is great in the laboratory but no good in patients."

We need additional patients and a longer period of follow-up to prove the worth of immunotherapy. However, the laboratory results are encouraging and we are hopeful that the procedure eventually will be useful as an adjunct to cancer surgery.

Immunology ultimately may be the tool we need to understand tumor specificity and to develop different therapeutic approaches said Dr. Gold. New avenues are opening up to increase cellular immune response with thymus extract. Who knows from which direction the cure for cancer may come. In the meantime all avenues should be explored.—L.H.N.

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Drug Abuse Overtaking Alcoholism As A Business Problem

Drug abuse may be emerging as a major problem in the business world according to a study carried out for the New York Chamber of Commerce by the Research Institute of America. In this study an attempt was made to establish the extent of the problem, to help companies with advice and information on the various types of drugs now in common use, the laws relating to them and finally the agencies available to deal with them.

A survey of eighty companies, many of them major American companies based in New York City has shown that only five had no incidence of drug abuse on the company premises. All five were small and had low employee turnover. The other companies reported that the incidence had skyrocketed in 1969, and that there were more than three times as many cases reported in 1970. Many companies believe that what they are seeing is just a preview of what the situation will be.

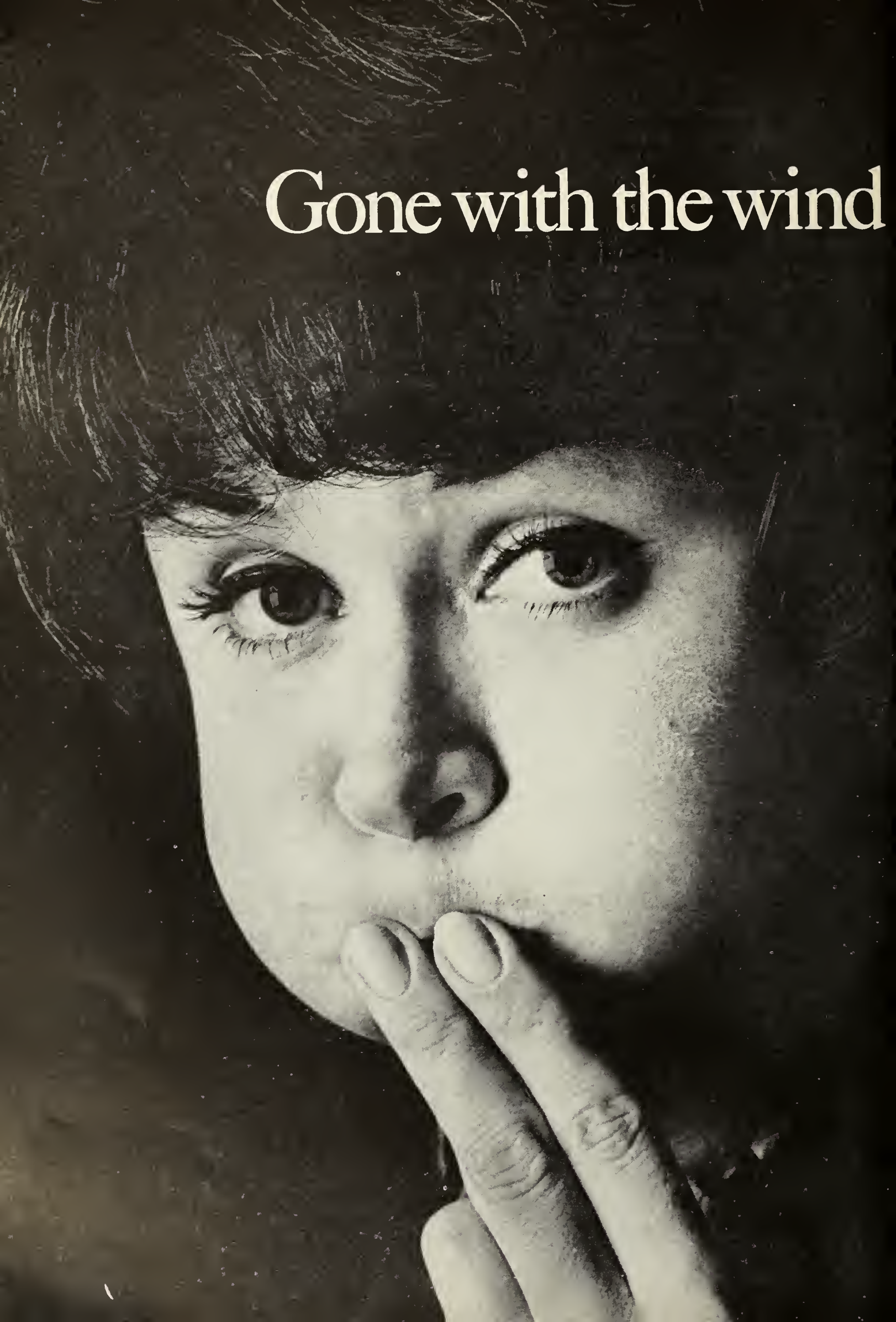
Most frequently cited as the major reason for the growing problem is the increase in employment from the hard core previously unemployed. However, the study also pointed out that the problem is not limited to the poor or to the young. As drug abuse has become more common and more accepted in recent years, it has affected employees at all social and economic levels.

With an estimated 100,000 heroin addicts in New York City alone, a growing number of people in their 20's and 30's using marijuana and over 500,000 people in the United States abusing barbiturates and amphetamine, it is not surprising that the abuse of these drugs is overtaking alcoholism as a business problem. Companies point out that drug abuse has resulted in higher personnel turnover, employee thefts, absenteeism, poor work performance, higher insurance rates and the general increase in taxes needed to handle the drug problem. Thus in the end, all society pays for handling the drug problem both in higher costs and higher taxes.

The turnover due to the release of addicted employees cost one company $75,000 in 1969. Another company reported a 100% jump in thefts by employees from 1968-1969, most of which was due to the increasing numbers of addicts working for them. Another company found that a company engineer was using the interoffice mail to distribute marijuana. Most companies have been slow to develop procedures for dealing with drug abuse and have often been caught unawares. The larger companies have responded most rapidly because they already have sophisticated health services with general policies covering mental health and alcoholism and have established procedures for recognizing a wide range of employee problems.

Companies in sensitive industries such as air lines, banks and manufacturing plants with dangerous equipment tend to feel that they cannot take chances with their customers, their employees or their public image. Once drug abuse of any kind, from heroin to marijuana has been determined, dismissal follows. Most firms, however, still find the decisions complex and difficult as they discover that drug abuse is anything but neatly categorized. Some are already making a distinction between the "soft drugs" such as marihuana and the "hard drugs" such as heroin and the other opiates.

While some companies are committed to a policy of automatic dismissal because of the sen-


Gone with the wind

sitive nature of their work, others think that they will be unable to do this in the future as the problem grows. Still others see themselves as part of the community and believe that they have to expand health services to meet changing social demands. The primary problem obviously is selection. Screening of employees by urinalysis to detect recent amounts of drugs in the system is not effective if a user has abstained from drugs for a few days prior to the test.

A urinalysis costs from 25-35 dollars and many firms have neither the facility for sophisticated medicals nor the funds to have this test run on every applicant. In any event many applicants slip through the screening test. One company reported that 25 per cent of its applicants in 1969 showed positive urine specimens. These, of course, were not hired, but a spot check a few months later revealed that 25 per cent of the group already hired were using drugs.

Since preventive detection is so often neither practical nor effective, the study stresses that the role of company supervisors in recognizing the symptoms of drug abuse easily and taking the appropriate action can be crucial.—L.H.N.

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Methods For Pest Control In Agriculture

The quality of the environment stands high among the problems demanding attention. Accordingly, we must prevent pollution of the air, land and water beyond a level man can and will endure. But the world is becoming more populous and one of the greatest needs is production of food for billions of people. At present such production requires the use of pesticides until a safe, effective substitute is found. At present pesticides carry with them the serious problem of environmental pollution.

The large acreage of wheat, corn or citrus orchards provide inviting environments for pests and disease of crops, big broiler flocks and cattle-feeding operations. These greatly increase the opportunity for animal diseases and pests to survive and spread. Were it not for pesticides the balance of nature would be heavily weighted on the side of the pests. At present the synthetic, organic pesticides which can be applied over large areas in a matter of hours, fit our efficient agriculture. Along with fertilizers, irrigation systems and complex machinery, they have made it possible for only 5 per cent of the American work force to meet the nation's needs for food and fiber.

This does not mean that the use of pesticides is the only available method for combating pests and disease. Nor does it mean that current pesticides must continue to be used in present quantities. It does mean that at present chemicals are the most effective weapons for pest control which the farmer has. The use of some pesticides will decrease and some will cease to be used altogether, although the total amount of chemicals used for pest control in agriculture can be expected to increase as the need for agricultural production increases.

The first step in avoiding pest problems is quarantine, keeping pests out of the country. This has protected us from many exotic insects and diseases such as the Mediterranean fruit fly.

Much of the research on pest containment and controls is now focused on development of resistant crop varieties; improvement in agricultural practices; the use of insect parasites, predators, and pathogens as biological agents. This is the development of genetic defects such as sterilization, physical devices, as well as more selective chemicals such as attractants and hormonal insecticides. Plant breeders have been successful in developing varieties resistant to certain disease notably wheat, corn, alfalfa and potatoes. But in some cases even the best of varieties so far developed are unable to resist massive infestations by insects and chemical insecticides become essential to provide effective protection.

Cultural procedures are also important to the farmers such as sanitation, early planting of crops, destruction of crop residues, tillage, crop and animal rotation, strip-cropping, destruction to volunteer plants, and specific harvesting procedures. Even so, they can be totally inadequate unless used in conjunction with chemical control.

Biological control involves the use of insect parasites, predators and diseases to prey upon the damaging pests, and thus control their numbers. Over 520 species of predators have been imported of which only 20 have provided significant control by themselves. For example, release of aphid lions was as effective against the ballworm as the available insecticides. In another study, 100 million parasitic wasps released on 18,000 acres of alfalfa suppressed population of winged aphids and protected 130,000 acres of peas from virus diseases. A polyhedrous virus which poses no hazard to man or other forms of life destroyed the cotton bollworm and the cabbage looper.

A flea beetle from Argentina was found to be a damaging enemy of the alligator weed which chokes reservoirs, canals, and waterways and has helped to control the weed in some areas. However, the complex problems to be overcome, notably the difficulty of mass producing biological agents indicate that we are still a long way from being able to depend on these methods for practical pest control.

Manipulation of insects for their own destruction by inducing sexual sterility or introducing harmful genetic traits hold considerable promise. Two methods of using sterility are being studied. One is rearing massive numbers of pest species, sterilizing them with gamma radiation, and releasing the insects to compete for mates in the natural population. The resulting eggs will not hatch, and the insect population dwindles. This method was used to eradicate the screwworm from the southeastern United States and is now employed to supress this livestock pest throughout the southwestern region of this country.

The second method involves application of chemosterilants to native populations at a central source after which the treated insects disperse and serve to reduce the reproduction of target pests in the environment. The sterility method is being used to replace insecticide spraying in preventing the entry of the Mexican fruit fly into California. This method has potential for suppression of boll weevil, corn earworm, tobacco budworm, cabbage looper, fall armyworm, and hornfly.

It is clear that in developing this method, scientists must have a thorough knowledge of the biology, ecology and population dynamics of each target insect. Mass rearing and sterilizing billions of insects are often needed to flood adequately the target insect population. Irving[1] also points out that the sterility technique is usually successful as a tool for eradicating and continuous suppression of an insect only when used in conjunction with other methods of pest control or when insect populations are reduced by natural causes.

One of the newest trends is research to identify and develop attractants and hormones for insect control. Naturally occurring attractants are highly specific in infinitesimal amounts. They need to be isolated, identified and then synthesized. Sex attractants have been demonstrated for a variety of major pests. The use of appropriate sex pheromones in combination with black light traps for the control of the tobacco hornworm and cabbage looper have been encouraging. The synthetic lure, methyl eugenol is now used to eradicate the oriental fruit fly.

Another recent trend is research on hormones and hormone-like materials that may be used as insecticides to disrupt insect development rather than to cause immediate death. Certain of these hormonal materials are effective against specific pests at fantastically small dosages. Recently, several new "hybrid" synthetic ethers, similar to juvenile hormones, are far more potent than the insect's own hormones and can be intensified 10 to 20 times more when combined with synergists such as sesamex.

It will, however, be some time before some of the many new chemicals under study will be ready for practical use.—L.H.N.

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Marihuana: 1

Marihuana is among man's oldest and most widely used drugs. It has been eaten, drunk, snuffed and smoked as long as medical history has been recorded and is currently used through out the world by hundreds of millions. The many published observations on marihuana users present a fairly consistent picture of its short term effects. With regard to long term effects, there are strongly contradictory opinions ranging from harmful to beneficial to human functioning.

It is estimated that 10 percent of the population have smoked at least once and the percentage is higher in the young. In Vietnam 32 per cent of the soldiers use it and 45 per cent of medical students have used it.[1] The users tend to be more individualistic, liberal politically not religious and somewhat impulsive. They are perceptive, sensitive to the need of others, have the motivation to succeed. Users in high school more often come from broken homes engage more frequently in sexual intercourse and are more often in trouble with the law. But their grades are as good as the nonusers.[2] Within deviant subgroups, marihuana use was high. However, overall the majority of users appeared to be reasonably conventional.

The intoxicating properties of cannabis resides in several tetrahydrocannabinols whose concentration depends upon the plant strain as well as soil and climate so that there can be a difference of 70 times between the most and least potent plants. In this country the two plants of importance are marihuana leaf and hashish. The leaf is pulverized, rolled into a thin cigarette or smoked in a pipe. Hashish, the pure resin in the form of a hard brown cake is usually smoked in a pipe. A cigarette containing 250 to 500 mg of leaf will produce a moderate to intense intoxication within 15 minutes. Hashish is up to 10 times as potent and is used in proportionately smaller amounts.

The literature contains many accounts of marihuana intoxication from Baudelaire to Allen Ginsberg.[3] Pillard's study of medical school student users concerned with the subjective effects they experienced from marihuana and alcohol. With marihuana they all reported feeling relaxation, tranquillity and many mentioned "increased awareness" of such sensuous experiences as food, sex and music. Other responses were a quietness of spirit . . . "I was fascinated with ideas and objects . . . like the world around me was a new place." Sounds envelop me and become more distinct . . . "more aware and compassionate of other people." Under the influence of alcohol they also felt more relaxed and at ease but tended to report "diminished awareness" "dulled senses" "muddled" "fuzzy" and "sleepy" were frequent descriptions.

Typically the user feels a series of jittery "rushes" soon after inhaling, a sense of relaxation and well-being follows. There is awareness of being intoxicated unlike that produced by alcohol. The user becomes acutely conscious of certain stimuli to the extent that his whole attention is focused, immersed and at times lost with the sensory experience. In this state jokes are funnier, misfortunes more poignant, and human relations more deeply perceived and more seriously misperceived."

The appreciation of food, sex, and in particular music is intensified. The user may believe that

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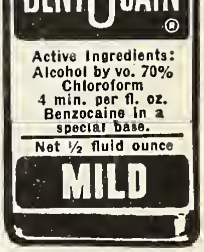

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his thoughts are unusually profound (an impression not shared by the observers). Paranoid thoughts and feeling of depersonalization have been reported by subjects and observed in the laboratory. Visual imagery is increased[4] and, in large doses, colors may shimmer and visual distortions occur, although this effect is not nearly so intense as with hallucinogens. There may be feelings of changed body proportion. Among the most striking perceptual changes is the subjective slowing of time. As vivid as these effects are to the one who is experencing them, the observer usually has little to observe. The subject may be laughing and gregarious or quiet and remote. His speech is often peculiarly disconnected. Mild states of intoxication, however, may be quite undetectable.

Three types of adverse reactions have been described. One type is that of reactive fright and panic. The smoker becomes apprehensive, fearful or panic-stricken. Paranoid thoughts get out of control and the smoker fears he is going insane. These reactions occur very rarely and subsides when the drug wears off. In contrast to their anxiety reactions are toxic psychoses, thought disorganization, paranoia, depersonalization and hallucinations that last for days or even weeks after the drug is discontinued. About one in ten had such ill effects in LaGuardia's studies.[5] Three of these were schizophrenics and the other six showed toxic delirium which subsided in a few hours. Others have reported suicides, psychoticlike states triggered by marihuana. We still need to learn the psychodynamic or physiologic factors that make some persons vulnerable to decompensation. Finally are the rare cases of "Flashback" found in LSD users but also reported after marihuana. This is a condition in which the subject suddenly feels the drug effect even though he has not used the drug for days or weeks. The cause is unknown.

The consistent physiological changes observed are tachycardia lacrymation, dry mouth, enhanced appetite. Temperature, blood pressure, respiration and pupil size do not change. Simple tasks such as tapping speed reaction time and continuous performance are not much changed. However the more complicated tasks such as digit symbol substitution and complex reaction time are obviously impaired. Also impaired is digit code memory, serial addition, figure closure and tasks that require physical co-ordination. Pillard states that there is a good deal of variability between subjects, the inexperienced users do less well.

The specific and characteristic effect on perceptual processes, have not been identified. The phenomenon that comes closest is the striking distortion of subjective time estimation.[6] Subjects will overestimate an elapsed time interval and when shown a clock will express surprise that so little time has passed.

These subjective effects ranged from practically none in some of Weil's naive subjects through the usual relaxation and euphoria to depersonalization, hallucinations and loss of reality testing with large doses.—L.H.N.

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Problems And Hazards Of Pesticides

There are high hopes and great enthusiasm for the eventual development of effective alternative means of pest control, but for the present we must depend on chemicals used selectively and prudently. Therefore, as we continue to use pesticides in agriculture, we must be aware of the problems and hazards that they can create for man and his environment.

Pesticides have their shortcomings. One is the development of resistance to the organochlorides by the insect pests. The most spectacular was the development of resistance to DDT and in some species each succeeding generation developed stronger resistance. The house fly and the boll weevil became almost impervious to the originally potent effects. Already 224 species of insects around the world have developed resistance to one or more of the insecticides. Of these, 127 are agricultural pests and 97 are pests of medical and veterinary importance.

The broad spectrum persistent pesticides affect many organisms other than the target pest. Some of the more specific pesticides in use today are more acutely toxic to man. Thus the long-term result of shifting away from broad-spectrum to specific pesticides may be creation of greater immediate hazard to man and the need for more chemicals than are now used.

The harmful effects upon man over the use of DDT and its relatives has become a matter of public concern and continues to grow largely because of another problem. Residues of DDT and related pesticides do not readily break down and instead dissipate very slowly. Residues have been accumulating in the environment, in adipose animal tissue and in milk. Residues of DDT have been found many miles from the point of use, for example, in tissues of polar bears and other wildlife in the Arctic.

The residues of DDT and its relatives are harmful to certain beneficial insects, including pollinators, parasites and predators of pests. Some fish and birds have been harmed by these residues. Species react differently to pesticides. For example, DDT can cause thinning of eggshells in ducks and falcons, but not in pheasants and quail. Pesticides from the air, water and soil may be absorbed and concentrated in the bodies of organisms. The concentration in the tissue is frequently increased as one species feeds on another and passes the pesticide from one link to another one higher in the food chain. In this sequence some predators, like birds and fish, may be exposed to levels several thousand times the concentration in the physical environment. Increased precautions are obviously necessary.

A guideline is emerging with which most agree. Persistent pesticides should be released into the environment only when absolutely necessary, that is, when the need is to protect human health or life-supporting food supplies and when no satisfactory alternative is available. Most also agree that research on the long-term effects of persistent pesticides in the environment should be intensified since, even with this guideline, we will continue to need and use some persistent pesticides.

Actions are being taken to accomplish an orderly reduction in the use of persistent pesticides without sacrificing essential uses. Now scientists carefully evaluate registration of chemicals proposed for specific uses. On November 25, 1969, HEW cancelled registration of DDT

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against pests of shade trees, tobacco, house and garden, and aquatic sites such as marshes and swamps. It announced its intention to cancel all other uses of DDT except those needed for prevention and control of human disease and other essential uses for which no alternative means of pest control are available.

On April 23, 1970, the Department of Agriculture announced that pesticide manufacturers and formulators had been notified that federal registration of certain 2,4,5-T products used for weed control is suspended. This is the herbicide which has caused ecological chaos in Vietnam and is strongly suspected of teratogenic effects on man. The suspended products include liquid formulations for use around the home, recreation areas, lakes, ponds and ditch banks. Without doubt less persistent chemicals should be used wherever possible.

To increase our criteria for safety, particularly for keeping the use of persistent pesticides to the minimum, we must ensure that judgment by the government agencies will be made on the basis of the best scientific knowledge available. In the case of pesticides, the process of arriving at knowledge is being hastened under the glare of the public spotlight in which scientific issues are being debated by scientist and alarmed laymen.

Basic to the speedy resolution of these controversial issues is more knowledge which can come only through research. For example, we need to know what the long-term effects of persistent pesticides on man will be. We need to know their ultimate fates in soil, water, and other parts of the ecosystem. Crucial to the resolution of questions of environmental pollution, particularly, as they concern pesticides, is the establishment of the significance in man of the results of toxicological experiments on laboratory animals.

We need to have settled, among other things, some questions concerning cancer and carcinogens, species specificity, significance of dose size and route and the other substances to which the living organism is concomitantly exposed. We need knowledge so we can cut through the present scientific complexities and arrive at an acceptable practical answer to the question, "how safe is safe enough?"

This is far from an academic question. It is one that must be faced repeatedly in administering programs for pest control and in regulating the use of pesticides. These decisions must be based on scientific knowledge and what is best for the overall welfare of man, his environment, and the creatures with which he chooses to share the environment. In performing these services the administrative agencies will be greatly helped by an informed public who watch carefully that the agencies perform their duty only in the public interest.—L.H.N.

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Water Pollution Abatement

No massive reductions in water pollution have occurred. Still there have been a few cases of successful pollution abatement—parts of the Farmington River in Connecticut, the Willamette in Oregon, and Lake Washington in Seattle, for example. Other encouraging signs are the work that is being done in sewage treatment and the construction of new sewage disposal treatment plants has been gaining on the population. From 1940 to 1962, the number of new facilities just kept abreast with or fell slightly behind population increases. Whereas from 1962 to 1968 the population served by sewers increased from 60 to 68 per cent.

The most significant advances, however, have been made in research and development for sewage treatment. In the last 10 years the government has put about $25 million into waste-water treatment studies. A recent article cites 85 processes being studied at more than 150 locations.[1] Of special interest are three pilot plants operated by the Federal Water Quality Administration (FWQA) and a 7.5 million gallon per day (mgd) advanced treatment plant operated in California by the South Tahoe Public Utility District.

About two trillion gallons of waters are used in this country each year to carry waste from industry, business and homes. After use this vast quantity of sewage is still 99.9 per cent pure water, but the contaminants cause deterioration in water quality of receiving rivers and lakes. For treatment purposes, the contaminants generally are considered as groups such as suspended solids, dissolved organics and dissolved inorganics. Nitrogen and phosphorus are dealt with separately besides the above three because of their role in eutrophication, a property of waste that particularly degrades natural waters is its ability of consume oxygen—its biological oxygen demand (BOD).

The sewage from a little less than a quarter of our population receives only primary treatment and the sewage from about 5 per cent of the population receives no treatment. Primary treatment consists simply of allowing the sewage to settle and separating the water from the sludge at the bottom and the scum on the top. Such treatment removes about 1/3 of the BOD and suspended solids and a few per cent of the refractory organic compounds and plant nutrients.

Sewage from about 40 per cent of the population gets secondary treatment. The most widely used methods now in operation are the trickling filter and activated sludge process. In the first process, effluent from primary treatment is allowed to trickle through a deep bed of rocks containing various microorganisms that utilize organic and nutrient materials in the sewage. In the second process, the microorganisms use up primary effluent materials in tanks through which air and preferably pure oxygen is passed.

Tertiary treatment, a form of advanced waste treatment, involves the use of chemicals that can be used for precipitation, flocculation as well as filter aids. The methods now being used to remove phosphates and nitrogen are still far from satisfactory and many are being tested in various parts of the country. One recent development with much promise is the discovery of a natural mineral, zeolite, which adsorbs both phosphates and nitrogen.

Sludge handling is by far the most difficult problem in sewage treatment. It costs almost half of the total cost and the numerous methods still in use indicate that there is no simple solution. We need much more knowledge in this area. The FWQA estimates that it will cost 10 billion to get domestic wastes up to recommended standards, and 3.3 billion for industrial uses, a relatively modest sum when compared with the amount spent in the Vietnam war. The battle against water pollution is far from won and the major difficulty is getting the money which means clarifying our priorities in the direction of health and welfare.

Holcomb points out that "the lack of reliable information on industrial water pollution control activities might be considered intolerable, if the nation had not become quite habituated to it . . . every effort to initiate an industrial waste inventory has been frustrated without noticeable public comment." Another difficult but important survey that is required is to determine the composition of water that runs directly from land to natural waterways, such as eroded soil and the waste from the agricultural industry that finds its way into rivers and lakes. It has been estimated that perhaps half of the phosphate in natural water comes from this source.

Finally, the problem of trace contaminants and health is not well studied. The recent series of discoveries of mercury contamination illustrates a process that has now been repeated several times. Routine water analyses are made only for major indicators of water pollution, so that measurable amounts of unusual substances can be present for long periods of time without being detected. Once a systematic search is made, some of the substances are found to be rather common. This happened with DDT, detergents, phosphates, and now it has been repeated with mercury.

What other poisons have we not looked for? The Waste Water Reclamation Committee of the American Water Works Association at their July meeting in Washington, D.C. cited the possible presence of the following substances as one reason for not utilizing reclaimed water unless other sources are not available: chemical and biological toxins, trace elements, pesticides, carcinogens, antibiotics, hormones, viruses, and materials not yet studied.

A broad-based research and development program in waste water is being pursued. Nevertheless, much work remains to be done. Monies must be made available, fundamental research problems must be solved and a major health catastrophe must be avoided by carefully monitoring our waters for small amounts of dangerous substances.—L.H.N.

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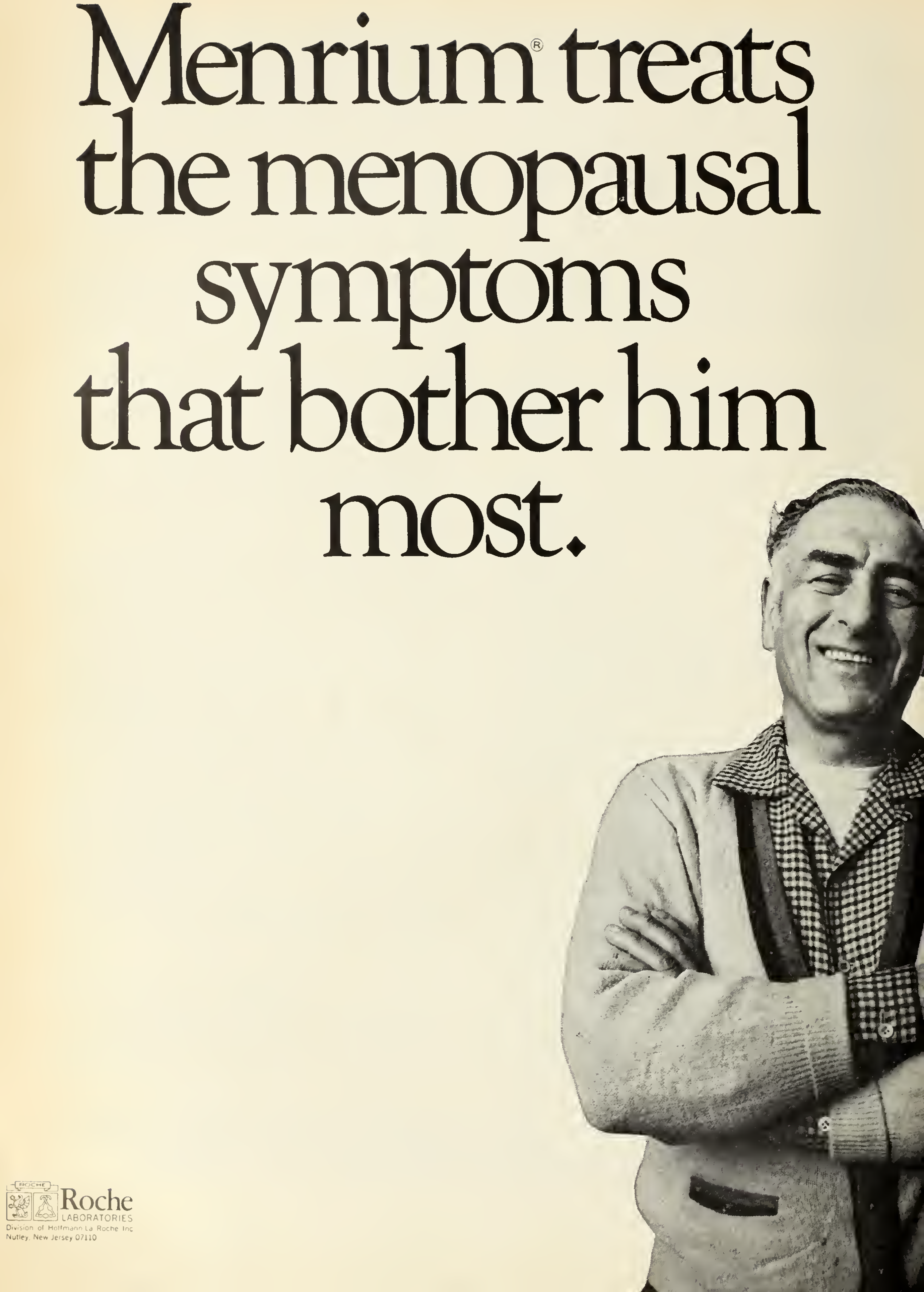

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Precautions: In elderly and debilitated patients, limit dosage to smallest effective amount of chlordiazepoxide (initially 10 mg or less per day) to preclude ataxia or oversedation; increase gradually as needed and tolerated. Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects—particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in patients with impaired renal or hepatic function. Paradoxical reactions to chlordiazepoxide (*e.g.*, excitement, stimulation and acute rage) have been reported in psychiatric patients. Employ usual precautions in the treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation very rarely reported in patients receiving Librium® (chlordiazepoxide) and oral anticoagulants.

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Environmental Causes Of Congenital Defects

There are approximately 15 million people in our country who were born with significant often crippling physical defects. In 9 million of these no causes have been found. We do know, however, that approximately 25 per cent of the physical congenital defects are hereditary and 75 per cent are environmental. The causes of environmental congenital defects are known for the most part; rubella, radiation including ^{131}I fallout, medication the mother takes during pregnancy and malnutrition of the mother during pregnancy, particularly protein inadequacy.

There are approximately 6 million mentally retarded persons in our country. In only one-fifth of these do we know the cause but we do not know the cause in the other four-fifths and so we say, "they were born that way". Many other millions of our people have serious psychiatric disorders. Again in most of these the causes are obscure.

It is a curious and almost unbelievable fact that the very early life of human beings has not been prospectively studied in depth, especially in relation to congenital disorders or in relation to health and disease in general. For example, it is believed that one person in 600 measles cases develop encephalitis. How many others had mild or transient involvement of the brain. How many virus infections lead to brain involvement and subsequent behavioral disorders. The fact is that we physicians have been practicing medicine and teaching medicine while inadvertently we failed to take into consideration the most important phases of life during which most of the congenital defects are produced by environmental factors.

To be sure there are excellent but only partially prospective collaborative studies of the National Institute for Neurological diseases and blindness. There are also important contributions of the National Foundation (March of Dimes). There are also elaborate permanent research and treatment conducted throughout our medical institutions. Nevertheless, medical histories as we take them on patients often fail to elicit or record the most important medical facts and completely ignore the patients first 20 years of life. This failure, of course, can be attributed to our misconceptions concerning the beginning of life of the next generation.

It is self evident that life begins in the germ cells which are derived from oogonia and spermatogonia; not at birth, not when a women presents herself for obstetrical care, not even at the time of conception. The germ cells are the threads of transmission that live on from generation to generation, transmitting eternally not only the genetic but the environmental factors as well. We somehow do not take sufficiently into consideration the following facts:

When a female child is born she has all the ova or precursors the oogonia in her ovaries that she will ever have. She does not make any more. The germ cells over the years are subject to environmental influence and probably collect mutations as their bearer grows older. When a male child is born he has millions of spermatogonia the precursor of spermatozoa in his testes. Even though we do not know whether after his birth he makes any new spermatogonia, however, the production of spermatozoa permits the non-functional damaged ones to be thrown off. This is why the male germ cells can remain viable in advancing years of their bearer, while the female ova may respond by mutations to environmental stimuli.

Germ cells are known to be highly vulnerable to environmental hazards, especially the ovum. According to Potter, from 1-2 million women in our country every year abort spontaneously, often unknowingly during the early days of pregnancy. Studies of these recovered embryos by Hertig and others have demonstrated that approximately 50 per cent were so defective that they could not survive. The causes for this tremendous wastage of early pregnancy are almost totally unknown.

Differentiation (formation of organs) occurs very early in pregnancy and is almost complete by the eighth week of gestation. After that there is rapid growth, but very little further differentiation. Thus the toll of injury, malformation, sickness and death of the fetus has already occurred often before a woman knows she is pregnant and long before she seeks prenatal or obstetrical care which is at about 21 weeks of pregnancy. It can be seen that the earlier in pregnancy an environmental impact occurs, the more profound is the effect on the conceptus.

The foundation of one's life then, that part upon which later life rests, begins in the living germ cell. None of our patients knows anything about that part of his life during its first 20 years. He knows nothing about the phases of preconception, conception, pre-embryonic, embryonic and his fetal life. Many patients know nothing or almost nothing about the problems of their birth, and delivery or about the neonatal period. Our current medical histories begin approximately 20 years after life began and hence fail to record the most significant facts. There is reason to believe that the ingredients of success or failure, physically, mentally and psychologically resides in the secrets of these unexplored years.

The Medical Passport Foundation has taken upon itself the task of providing a protocol for exploring prospectively for the first time in a pilot study this hitherto unexplored medical contingent. It believes that the medical history of the next generation should begin at the time of contemplated conception. At this time elaborate examination of the male as well as female partners should be done, and the five phases noted above should be entered into a medical history.

As a result of such a study of early life when correlated with the events of later life, it is believed that much more than we now know will be revealed about the causes of congenital defects and hopefully that this will be converted into prevention. When one can compare the patterns of early life with the patterns of later life, it seems probable that we may learn not only the patterns of early life that make one unsuccessful physically and mentally, but also unveil the patterns of early life that result in the superior person, physically and mentally. Since our human material is our greatest resource, it is time we began to think of ways to achieve superior human beings.

By the documentation of very early life, it seems entirely possible that we may give to psychology and psychiatry what they have been searching for. From the beginning they have retrospectively probed the past with a variety of tools, psychoanalysis, "truth" serums, Rorschach tests, analyses of dreams, hypnosis and tranquilizers, because they believe something hidden, submerged, forgotten or perhaps never known, must have happened in the early life of the patient to have caused him to think or behave abnormally. One objective approach to psychiatry might come from the history as is being obtained by the protocols of the Medical Passport Foundation.—L.H.N.

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How Much Superstitution In Our College Students

There appears to be a growth of superstitious subculture in the United States including increased popular interest in horoscopes. In order to determine whether a university education has any effect on traditional supernatural beliefs held by many students at the University of Ghana, Yahoda studied many students and concluded that there was no evidence that education as it is practiced today even including scientific training had any discernable impact on their magicomythical beliefs. He therefore suggested that if such beliefs impede the growth of science in developing countries then methods other than general education must be used to diminish them.

Yahoda studies led Pasachoff et al, to attempt a similar investigation on undergraduates at Harvard to try and understand the African studies as well as the situation in our own "backyard". Two hundred male students at Kirkland House of Harvard College answered a questionnaire containing nine questions. With instructions explaining that O indicated total "unqualified belief", they were asked whether they believed in astrology, extra-sensory perception, flying saucers and the power of prayer. They also asked two questions whether science could ever predict "human actions" and all physical occurrences but set the answers to these questions aside because of ambiguous phrasing. Students were also asked whether they crossed their fingers to bring themselves luck, "knocked on wood" or walked under ladders with O indicating never and 20 indicating always.

Selection effects were negligible and students were answering honestly. The average belief in astrology was low 2.5 on a scale of 20. However, extra-sensory perception was as much as 11.9, flying saucers 8.5 and power of prayer 8.5. Thus many students at Harvard as in Ghana do not reject the supernatural although they do not accept such fixed beliefs as astrology. But even in astrology although 161 indicated disbelief 16 were neutral and nine assessed their belief at 75 per cent. Only 35 per cent were nearly certain that flying saucers do not exist while 30 per cent were neutral and 20 per cent were strongly believers.

Students of the natural sciences believed markedly less than their fellows in astrology, extrasensory perception and flying saucers. There were no clear differences between students of the humanities and social sciences which leaves one wondering whether social sciences are being taught as "sciences". Natural scientists also seem less believers in the power of prayer although the fluctuations in these data are higher and hence the conclusion is less significant. One paradox was that students of the biological sciences tended to have higher belief scores than their natural science peers. There was also no obvious correlation with number of years of university education.

The students replied that they almost never crossed their fingers to bring themselves "luck" or knocked-on-wood with assessments of 27 to 35 respectively. There was a symmetrical distribution of answers to the questions about walking under ladders which may very well reflect an ambiguity in the wording of the question although it could also reflect a cultural habit.

Thus a sizeable fraction of the well educated students under study do not reject beliefs in supernatural explanations although the scientists tended to be more sceptical. However, the overall level of superstition is sometimes substantial among Harvard students. At the University of Ghana where Yahoda found "mean belief scores" between 5-8 on a scale of 20 his data showed that the science students did not differ from the overall sample as they tended to at Harvard.

What we need now to find out is whether the superstitions remain or gradually disappear under the impact of a science education and science practice. We need also to establish the kind of education our children will need to combat the superstitions they carry with them to college and perhaps throughout life.—L.H.N.

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Peer Evaluation Of The Office Laboratory

Every physician who maintains or supervises an office laboratory wishes to maintain high standards of test performance. Although there is presently no governmental regulation of office laboratories public health officials have scrutinized them carefully. In a statement to the Senate Judiciary Subcommittee on Antitrust and Monopoly (Feb. 1967) Dr. Morris Shaeffer of the New York City Department of Health asserted "With perhaps a few exceptions the worst of all laboratory work is done in the private doctor's office". In an attempt to study the validity of this statement the Oklahoma State Medical Association, using survey material provided by the College of American Pathologists, sent samples to 25 Oklahoma clinics representing 235 practitioners. This was done in March, May, August and October 1969. Of 1176 reported values 12.7 per cent were technically unacceptable and only 5.7 per cent were regarded as medically misleading. Results for bacteriology, serum calcium and serum uric acid were frequently poor but for most commonly performed tests were better than 95 per cent medically acceptable, far superior to what is implied in Dr. Shaeffer's testimony.

Larger laboratories supervised by pathologists have participated in College of American Pathologists Proficiency surveys for a number of years, and this has improved uniformity of analyses across the United States to a substantial degree. Although this is a non-governmental survey it is accepted by the National Chronic Disease Center as meeting Federal specifications for proficiency testing. Over 5,000 laboratories used this service in 1970. One great advantage of the large number of participants is that peer evaluation by method for each constituent analyzed can be carried out on a statistically valid basis.

The special CAP Peer Evaluation Program for office laboratories is an excellent way of checking office laboratory performance and comparing results with those of other office laboratories and those of referees. The 1971 program offers the following stable materials for analysis four times, in April, June, August and October.

2 vials for chemistry testing with specific levels for glucose, bilirubin, cholesterol, urea nitrogen and uric acid.

2 vials for hemoglobin
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    Protein
    Reducing substance
    Bile
    Hemoglobin

After the office laboratory submits its results for those tests performed it receives a computer printout indicating whether the results are acceptable and how they compare with those of other laboratories using similar analytic methods. For office laboratories performing any considerable number of the tests listed the $80. expense is a worthwhile investment. This type of program supplements but does not replace quality control programs based on either locally prepared or commercially produced stable material.

Participation in the CAP program can be arranged through the College of American Pathologists, 230 North Michigan Avenue, Chicago, Illinois 60601. Enrollment ends February 15, 1971.

R.N.B.

ANTICONVULSANT DRUGS IN IDIOPATHIC EPILEPSY

The standard anticonvulsant drugs, phenobarbital and diphenylhydantoin, used separately or in combination, can provide reasonably effective and safe control of seizures in more than three-quarters of all patients with idiopathic epilepsy of the grand mal, focal, and psychomotor (limbic system) types. Since the newer anticonvulsant drugs are more toxic or carry the risk of still undiscovered adverse effects, the doses of phenobarbital and diphenylhydantoin should be increased to the maximum the patient can tolerate, or if necessary the two drugs should be used together, before other drugs are tried.

PHENOBARBITAL—Phenobarbital is the safest and least expensive of the anticonvulsants, and is the drug of choice for infants and young children. The usual dose is 3 to 5 mg/kg daily administered in two doses. Drowsiness is the most common side effect; fixed drug eruptions occur occasionally. Because its effects on liver enzymes speed the metabolism of oral anticoagulants, patients taking both drugs require careful adjustment of dosage of the anticoagulant.

DIPHENYLHYDANTOIN (Dilantin – Parke, Davis; and other brands)—Most Medical Letter consultants recommend diphenylhydantoin as the first-choice drug for older children and adults and the alternative to phenobarbital for younger children. The usual daily dosage is 4 to 7 mg/kg given in one or two doses. When safe seizure control is difficult, dosage adjustment to provide a serum concentration of about 1 to 2 mg/100 ml or 10 to 20 mcg/ml may be necessary.

Ataxia and gingival hyperplasia are the most important adverse effects. If the gingival hyperplasia—probably an allergic manifestation—is marked, the drug may have to be stopped. Nystagmus appears when the plasma level is more than 2 mg/100 ml. The most frequent limiting toxic effect of the drug is ataxia, which is usually associated with large doses and a plasma level of 3 mg/100 ml or more (H. Kutt et al., Arch. Neurol., 11:642, 1964). Liver disease or interaction with other drugs, including isoniazid, aminosalicylic acid, phenothiazines, and dicoumarol, may depress normal metabolism and cause toxic reactions. Exfoliative dermatitis, probably due to hypersensitivity, has been reported. Granulocytopenia and aplastic anemia are rare, but a mild macrocytic anemia occurs occasionally. The drug can cause hirsutism in young women. A lupus erythematosus syndrome, mild hepatitis, generalized lymphadenopathy or a lymphoma syndrome, and peripheral neuropathy have been reported, though rarely.

OTHER DRUGS – Primidone (Mysoline – Ayerst) is a third-choice drug after phenobarbital and diphenylhydantoin. Studies have shown that about 25 per cent of it is metabolized to phenobarbital. Many clinical studies attest to its value in epilepsy, particularly for psychomotor seizures, but there is nothing in these studies to warrant its trial in the common types of idiopathic epilepsy before a trial of diphenylhydantoin or phenobarbital. Several Medical Letter consultants have found it to be very useful when combined with diphenylhydantoin, but not with phenobarbital.

Mephobarbital (Mebaral-Winthrop), like primidone, is metabolized to phenobarbital. There is no acceptable evidence that it is more effective or produces less drowsiness than phenobarbital in equivalent doses. *Metharbital* (Gemonil-Abbott) is metabolized to barbital, and its effects are probably due to the barbital.

Although *mephenytoin* (Mesantoin-Sandoz) is as effective as diphenylhydantoin in recommended doses, it has caused many cases of granulocytopenia, aplastic anemia, and exfoliative dermatitis. It should, therefore, be used only when the less injurious drugs have failed. White-blood-cell counts must be done regularly every two to four weeks for a year and then at intervals of not more than three months.

Ethotoin (Peganone-Abbott) is less effective than diphenylhydantoin and is not recommended by any Medical Letter consultant. *Acetazolamide* (Diamox-Lederle), a carbonic anhydrase inhibitor, may occasionally be useful in combination with other anticonvulsant drugs. *Phenacemide* (Phenurone-Abbott) is effective, particularly against psychomotor seizures, but it frequently causes such serious adverse effects as agranulocytosis, severe liver injury, and psychosis.

PETIT MAL EPILEPSY—The term "petit mal" should be restricted to seizures characterized solely by brief lapses of consciousness, absence of any except minimal abnormal movement, and onset in childhood. It should not be confused with the brief psychomotor seizures of adults. Petit mal seizures are readily precipitated by hyperventilation and are almost universally accompanied by electro-encephalographic 3-per-second spike-wave activity. Control is often difficult.

Ethosuximide (Zarontin-Parke, Davis) is probably the most effective single drug for petit mal epilepsy, though J. G. Millichap, who has had extensive experience in the management of epilepsy, prefers a combination of acetazolamide with mephobarbital (Mod. Treatm., 6:1217, 1969). Ethosuximide often causes drowsiness, ataxia, and other central-nervous-system disturbances; rashes are also frequent. Laboratory evidence of hepatic or renal dysfunction has often been reported, but serious liver or renal injury is rare. Blood dyscrasias have also been reported. *Methsuximide* (Celontin-Parke, Davis) has essentially the same properties as ethosuximide. Medical Letter consultants use *phensuximide* (Milontin-Parke, Davis) as the third choice of the succinimide drugs. When patients with petit mal epilepsy also have grand mal seizures, other agents must be used in combination with the petit mal drugs.

Trimethadione (Tridione-Abbott), formerly a favorite drug in petit mal epilepsy, is now used chiefly in patients who do not respond to or cannot tolerate a succinimide drug or the combination of acetazolamide and mephobarbital. The most common adverse effects of trimethadione are photophobia and drowsiness. Because the drug can cause nephrosis and aplastic anemia, examination of the urine for evidence of nephrosis and frequent blood counts are essential (see The Medical Letter, Vol. 11, p. 59, 1969 for a discussion of laboratory studies in bone-marrow disorders). Hepatitis, alopecia, a lupus erythematosus syndrome, and rashes or exfoliative dermatitis are less common adverse effects. The drug should be withdrawn if any of these adverse effects occur. An analog of trimethadione, *paramethadione* (Paradione-Abbott), while less toxic, is also less effective.

WITHDRAWAL OF ANTICONVULSANT DRUGS — Withdrawal should be gradual, since abrupt withdrawal sometimes brings on status epilepticus. In children, several Medical Letter consultants believe that therapy should be stopped after two of three seizure-free years, provided the electroencephalogram is normal. In adults, anticonvulsant therapy generally has to be continued throughout life.

STATUS EPILEPTICUS OR PROLONGED SEIZURES — Diazepam (Valium-Roche) is the drug of choice for status epilepticus. The dosage range for older children and adults is usually 5 to 30 mg, administered intravenously and slowly. For infants, 1 or 2 mg may suffice. In the recommended dosage range, diazepam can depress respiration and blood pressure; it should, therefore, be used with special caution if other anticonvulsants have previously been administered, since the respiratory-depressing effects are additive. The action of diazepram is brief, and repeated administration may be necessary. Equipment for maintaining an airway and assuring adequate respiration, by mechanical means if necessary, should be available. Medical Letter consultants emphasize that the drug is useful only in bringing status epilepticus under control, and not for the routine treatment of grand mal, focal, psychomotor, or petit mal epilepsy.

Some clinicians use 100 to 250-mg doses of diphenylhydantoin intravenously in status epilepticus, but others believe that it is less reliable than diazepam and that it has a greater tendency to produce vasodepressor effects. Sodium phenobarbital administered intravenously in a dose range of 50 to 400 mg (depending on age, weight of the patient, and severity of the syndrome) has also been effective. Either diphenylhydantoin or sodium phenobarbital can be safely given within about 60 minutes after diazepam has been tried and failed. All drugs for status epilepticus should be administered intravenously slowly over a period of many minutes, with special attention to respiratory and cardiovascular function. Some clinicians prefer paraldehyde to terminate status epilepticus; it is administered in doses of 0.2 to 0.4 ml/kg by rectum, or intravenously in saline solution. Because paraldehyde interacts with some plastics, plastic equipment should not be used.

OTHER CONVULSIVE DISORDERS—Hypsarhythmia of infancy usually responds to treatment with ACTH (20 units of Acthar Gel [Armour] daily for 20 days) or to diazepam. J. G. Millichap (cited above) recommends diazepam for myoclonic epilepsy; this disorder should be managed in consultation with a specialist in the treatment of epilepsy. A single febrile convulsion occurring within six hours of onset of fever in a child seldom requires anticonvulsant therapy. When therapy is needed, administration of diazepam or phenobarbital in appropriate doses is usually effective. A febrile convulsion is sometimes the first sign of epilepsy in a child.

Seizures, including status epilepticus, that result from head injuries can be treated with the same drugs as those used for idiopathic epilepsy. The control of increased intracranial pressure is usually more urgent than the administration of drugs for control of seizures following head injuries (Medical Letter, Vol. 12, p. 47, May 29, 1970).

CONCLUSION – Complete control of seizures, though often difficult to achieve, should be the aim of therapy. Less than complete control should result in a search for a more effective dosage schedule, which may require determination of blood levels of the drug being used, or for a more effective alternative drug or combination of drugs. Diphenylhydantoin and phenobarbital remain the most effective drugs for grand mal, focal, and psychomotor epilepsy, ethosuximide for petit mal, and diazepam for status epilepticus. Because all of the drugs used to control epilepsy can cause drowsiness, patients should be advised to exercise caution in the use of cars and power tools.

Reprinted from *The Medical Letter On Drugs and Therapeutics,* New York, N.Y., Vol. 12, No. 13, June 26, 1970.

States Sue Auto Makers

(*Science* 169: 659, August 14, 1970.) Fifteen states have filed suits in the Supreme Court to force auto manufacturers to install at their own expense pollution control devices on all cars sold since 1953, and to start a "crash program" to develop better devices and a pollution-free engine "at the earliest feasible date."

The states charged that General Motors, Ford, Chrysler, American Motors and the Automobile Manufacturers Association conspired to eliminate competition in pollution control devices and that such conspiracy violates the Sherman Anti-Trust Act.

The Justice Department brought a similar suit against the auto makers last year, but settled it with a consent decree under which the manufacturers agreed not to obstruct development and installation of the devices.—L.H.N.

Mercury Pollution

(*Science* 169:451, July 31, 1970) The Justice Department has authorized civil suits against 8 companies named by the Interior Department for allegedly dumping mercury into waters of seven states. U.S. District Attorneys will seek injunctions against the continued discharge of mercury under provisions of the 1899 Refuse Act. The act forbids the dumping of refuse into navigable waters unless authorized by the Army Corps of Engineers.

Civil injunction instead of criminal injunction procedures will be used because the penalty under criminal action is relatively light.

The suits will be filed against companies in Alabama, Delaware, Georgia, Kentucky, Maine, New York and Washington.

Mercury has recently been found in significant amounts in fish or waters of at least 13 additional states.

Vermont and Alabama have halted commercial fishing. Meanwhile commercial fishermen have field at least three lawsuits against plants for allegedly damaging the livelihood of fishermen and the United Auto Workers is considering filing suit on the ground that halting fishing deprives union members of recreation.—L.H.N.

Foreword

The Connecticut Society of American Board Surgeons is a unique surgical organization which was founded in 1948 for the purpose of promoting cooperation, education, and fellowship and to exercise a guiding influence on the development of surgery for the benefit of the people of Connecticut. Membership is open to any surgeon living in Connecticut who expresses a desire to join and who holds a certificate from the American Board of Surgery.

The annual meeting of the society was held in Wallingford on December 3, 1969. This issue of *Connecticut Medicine* contains manuscripts of eight papers presented at that meeting and a condensed version of some of the discussion which followed each paper. The subject discussed ranged from world-wide surveys to laboratory research and biochemistry, thus illustrating the breadth of subject matter now of concern and interest to the general surgeon.

Contributions were presented by surgeons representing several medical centers. If I may be allowed an editorial comment it would be that the purposes of the founders were well served by the vigorous discussion, the close communication, and the warm fellowship of surgeons from all areas of the state.

I would like to thank the contributors and the discussers for their cooperation in the preparation of this material for publication. It has been a pleasure to work with them and their contributions have required little editing. I believe that these papers represent a significant addition to surgical knowledge.

James H. Foster, M.D., *Guest Editor*

Operative Management of Esophageal Atresia By End-To-Side Anastomosis and Ligation Of the Tracheo-Esophageal Fistula

Robert J. Touloukian, M.D. and Lawrence K. Pickett, M.D.

The management of infants with esophageal atresia and distal tracheoesophageal fistula has passed through four definable stages since this major congenital anomaly of the esophagus was first described by Thomas Gibson in 1697.[1] Until 1939 all attempts at primary closure of the fistula with esophageal anastomosis and indirect methods of treatment combined with gastrostomy were unsuccessful. However, in 1939 Levin[2] and Ladd[3] working independently in Minnesota and Boston divided and closed the tracheo-esophageal fistula of infants on successive days. This procedure in conjunction with cervical esophagostomy and tube gastrostomy allowed the growth of the baby until esophageal replacement operations, including antithoracic skin tubes and colonic interpositions was possible. While a number of these infants were saved, function of the reconstructed esophagus remained poor and often the patients required permanent gastrostomies. Just two years following reports of the first survivors, the modern era of esophageal atresia surgery was made possible by Cameron Haight[4] who successfully treated a full-term infant by division and closure of the fistula with end-to-end anastomosis of the proximal and distal esophageal segments. With minor modifications, which included a variation of anastomotic techniques, a trend to preliminary tube gastrostomy under local anesthesia, and more adequate pre and post-operative care, the survival rate of full-term infants who had esophageal atresia and distal tracheo-esophageal fistula without severe associated anomalies rose to about ninety percent.[5] Unfortunately, the mortality rate of premature infants treated by primary anastomosis and the high incidence of esophageal complications remained of considerable concern to the pediatric surgeon. These problems were brought into clear focus through a cooperative study of 1058 of their patients sponsored by the Surgical Section of The American Academy of Pediatrics in 1964.[5] Since that time, most surgeons have staged the repair in premature infants by limiting the initial procedure to tube gastrostomy followed by extra pleural division of the fistula.[6] By adequate sump suction of the proximal esophageal pouch, the infants can be safely fed by gastrostomy until large and mature enough to tolerate an elective esophageal anastomosis. Lengthening of the proximal pouch by bougineoge is also possible during this period when the esophageal segments are widely separated.[7] This approach has largely eliminated the necessity for jejunal or colonic interposition operations.

The problems of esophageal stricture and late dyskinesia of the esophagus in the full-term infant treated by primary anastomosis also appears in large part to be eliminated by an increasingly popular modification of the esophageal anastomosis. This operation employs ligation of the tracheo-esophageal fistula in conjunction with an anastomosis of the end of the proximal esophageal pouch to the superior aspect of the side of the distal esophageal segment just beyond the ligature. This report summarizes the results of this operation in six infants at the Yale-New Haven Hospital between October of 1967 and June of 1969.

Preparation and Operative Technique

Once the diagnosis of esophageal atresia is made by esophageal intubation and confirmed by radiographic studies, the infant is promptly placed in an isolette supplied with cool mist. Adequate tracheobronchial toilet is maintained by repeated pharyngeal suctioning, or with an indwelling esophageal sump suction tube, combined with elevation and positioning of the infant. Antibiotics are routinely administered in all infants suspected of aspiration,

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either by clinical or roentgenogram findings. The operating room is readied for a tube gastrostomy which is performed under local anesthesia to reduce the possibility of further aspiration across the distal tracheo-esophageal fistula. A thoracotomy may follow immediately thereafter in the absence of systemic hypothermia or significant atelectasis or pneumonia. The infant is re-positioned for a right thoractomy upon induction of general anesthesia and a sub-scapular postero-lateral incision made to expose the retro-pleural area in the fourth intercostal space. The pleura is dissected until the proximal and distal esophageal segments are identified within the areolar tissues of the posterior mediastinum. The azygous vein is divided when necessary. A #2-0 silk ligature is passed around the tracheo-esophageal fistula. Care is taken not to mobilize the distal esophageal segment or injure individual esophago-aortic vessels. A twig of the vagus nerve passing to the esophagus should also be carefully preserved. The proximal esophageal segment is then mobilized until adequate length is attained to permit anastomosis of its end to the superior aspect of the distal esophagus. Anchoring sutures of #3-0 silk are placed between the proximal and distal esophageal segments. These delimit the margins of the anastomosis and correspond to the width of the proximal esophagus. When the anchoring sutures are tied the esophageal segments are opened obliquely between the sutures. Advancement of a naso-esophageal catheter will help to identify the mucosal lining of the proximal segment which is usually thick walled. A single layer anastomosis is then performed using interrupted inverted #4-0 silk sutures through all layers of each segment. A #10 to #12 Pezzar catheter is sutured to the chest wall about 1 cm. from the anastomosis with a #5-0 plain catgut suture and brought out through the posterior aspect of the incision to underwater seal. After the lung is totally expanded the ribs are reapproximated with interrupted #2-0 peri-chondral catgut sutures and the thoractomy incision closed in layers with interrupted fine silk. The infant is returned to the humidified and warmed isolette upon extubation of the trachea. (Fig. 1, a-f)

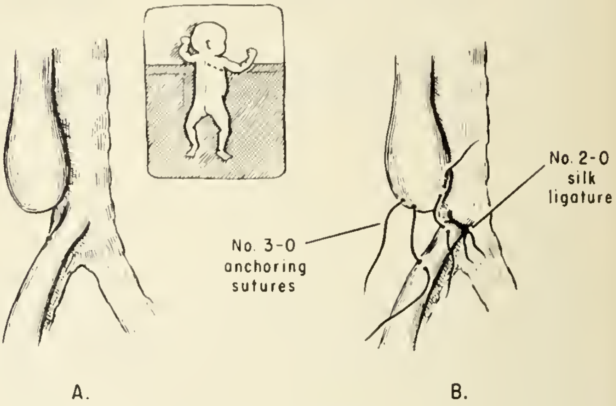
Case Material

Operative Management:

During the period between October 19, 1967 and June 18, 1969 six infants, including four males, with esophageal atresia and distal tracheo-esophageal fistula were admitted to the Newborn Special Care Unit at the Yale-New Haven Hospital during the first twenty-four hours of life. (Table 1). Their birth weights ranged between 2125 grams and 3062 grams. Each infant received aqueous crystalline penicillin K

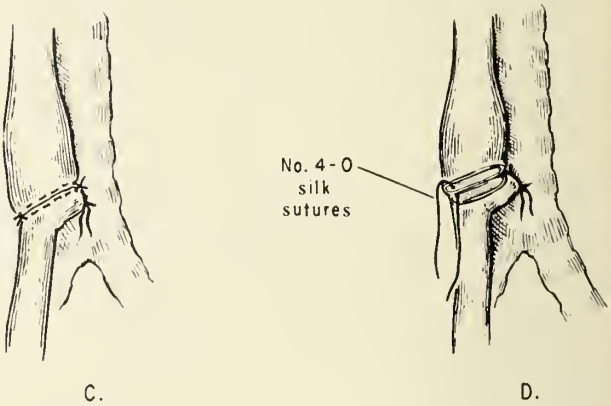
Figure 1

Operative management of esophageal atresia by end-to-side anastomosis and ligation of the tracheo-esophageal fistula.



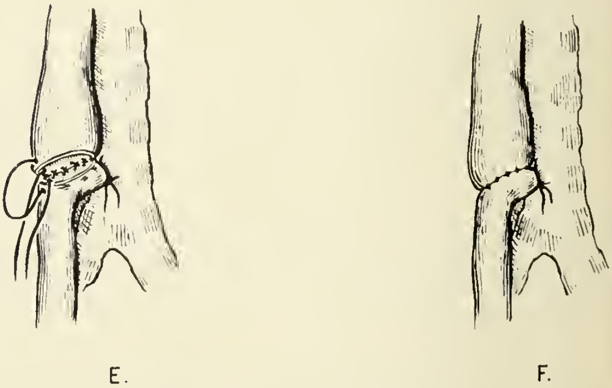
A. The usual type IIIb anomaly viewed from the right posterolateral approach.

B. The tracheo-esophageal fistula is ligated. Anchoring sutures delimit the breadth of the anastomosis.



C. The proximal and distal esophagus are opened after the anchoring sutures are tied.

D. The anastomosis is begun with simple interrupted sutures through the full thickness of the esophagus.



E. And completed with inverting sutures.

F. The result is an oblique anastomosis.

TABLE 1

CLINICAL SUMMARY

Case	Sex	Weight (Grams)	Age on Admission (Days)	Age at Gastrostomy (Days)	Age at TEF Repair	Discharged	(7-7-69) Associated Anomalies	Long-term Follow-up
1. D. D. #70-54-29	M	2840	1 (10-19-67)	1	3	59 (Expired 12-16-67)	Agenesis, left lung, Downs Syndrome (Trisomy 21)	1. Organizing enterocolitis 2. Mediastinal shift to left 3. Herniation of right upper lobe into left chest
2. R. C. #72-35-20	M	2125	1 (6-17-68)	1	2	21 (7-8-68)	None	Gastro-esophageal reflux with mild peptic esophagitis and anemia
3. T. P. #72-76-23	F	2600	1 (8-4-68)	1	2	17 (8-21-68)	None	
4. R. T. #74-42-73	M	3062	1 (2-27-69)	1	2	36 (4-5-69)	Hydronephrosis (Nephrectomy 3-7-69)	Tracheal stenosis after tracheostomy Pneumonia x 2 (5-8 and 7-2-69)
5. L. D. #75-01-92	M	2925	1 (5-15-69)	1	1	18 (6-3-69)	None	
6. I. B. #73-32-01	F	2400	1 (6-18-69)	1	2	19 (7-7-69)	None	Well

and Kanamycin (15 mb/kg/per day) in divided doses upon admission, although clinical signs of pneumonia were detected in only one infant. All patients underwent tube gastrostomies performed under local anesthesia within twelve hours of admission. The primary end-to-side esophageal anastomosis with ligation of the tracheo-esophageal fistula was carried out through an extra-pleural approach on the third day of life in one patient, the second day in four patients, and immediately following tube gastrostomy in the sixth patient. The fistula was ligated with #3-0 silk in two patients, #2-0 silk in three patients and #1-0 silk in one patient. A single layer anastomosis was performed with #3-0 silk in four patients and #4-0 silk in two patients. (Table 2) The patient with clinical evidence of pneumonia pre-operatively was noted to have moderate laryngeal stridor and excessive tracheo-bronchial secretions on extubation and a

TABLE 2

OPERATIVE MANAGEMENT

Case	Operative Approach	Type of Anastomosis	Fistula	Anastomotic Complications	Dilatations	Other Factors
1. DD	Extra-pleural	Single layer No. 3-0 silk end to side	No. 2-0 silk	None	None	
2. RC	Extra-pleural	Single layer No. 3-0 silk end to side	No. 2-0 silk	Minor leak 5 days	None	
3. TP	Extra-pleural	Single layer No. 3-0 silk end to side	No. 2-0 silk	None	None	
4. RT	Extra-pleural	Single layer No. 3-0 silk end to side	No. 1-0 silk	Minor leak 10 days	None	Tracheostomy for pneumonia (2-18 thru 3-11-69)
5. LP	Extra-pleural	Single layer No. 4-0 silk end to side	No. 3-0 silk	Minor leak 3 days	None	
6. IB	Extra-pleural	Single layer No. 4-0 silk end to side	No. 3-0 silk	None	None	

tracheostomy was performed immediately and removed on the tenth post-operative day. This infant was readmitted at two-and-one-half months of age and five months of age with right middle lobe and left lower lobe pneumonia treated successfully with antibiotics and pulmonary therapy. Repeat cine esophagram studies were normal. Moderate stenosis of the sub-glottic trachea was evident on lateral chest X-ray and possibly represented a complication of the tracheostomy.

Tube gastrostomy feedings were instituted on the second post-operative day. Five infants were swallowing salivary secretions by the second day, while the sixth required repeated pharyngeal suctioning until the sixth post-operative day. Oral feedings beginning with less than fifteen ccs of an electrolyte mix were begun during the eighth to tenth day in all patients, and increased by increments on a daily basis. Pre-feeding esophagrams were not obtained. Three infants developed anastomotic leaks during the fifth and seventh post-operative days with drainage of saliva and gastric contents for three, five and ten days thereafter. These infants were managed by gentle extra-pleural catheter suction. The suction drain was electively removed on the seventh post-operative day in the patients without complication and after drainage spontaneously ceased in the remaining infant.

Associated Anomalies:

Major associated congenital anomalies were noted in two patients. The first patient of this series had agenesis of the left lung (Figure 2) and Downs syndrome while the infant requiring tracheostomy had a hydronephrotic right kidney and underwent uncomplicated nephrectomy on the sixth post-operative day. The infant with agenesis of the lung expired on the fifty-ninth day with progressive dyspnea and signs of progressive pulmonary failure. Throughout this period, however, oral intake was excellent. Autopsy findings included a shift of the mediastinum to the left accompanied by herniation of the right upper lobe into the left chest. Small region of hemorrhage were noted in the right lung. The esophago-esophagostomy was well healed and the fistula replaced by fibrous tissue. A shallow diverticulum of the esophagus formed by the ligated fistula was visible from within the esophagus. (Figure 3)

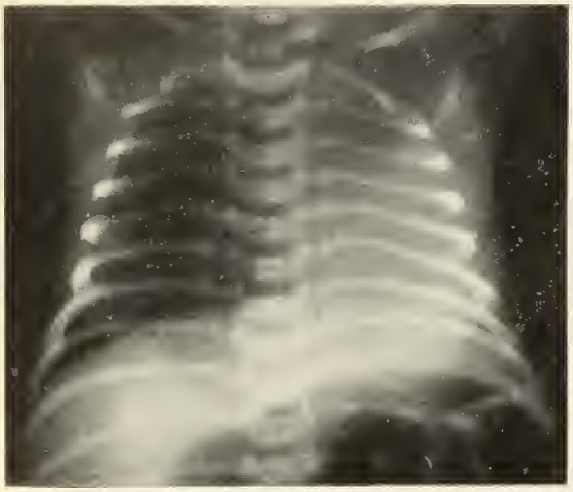


Figure 2

Ipsilateral displacement of the mediastinum in newborn infant with agenesis of the left lung and esophageal atresia.

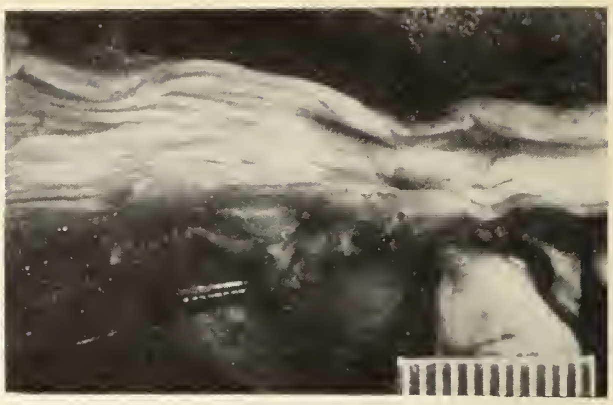


Figure 3

Well-healed esophago-esophagostomy almost two months following operation. The ligated fistula forms a shallow diverticulum visible from within the lumen.

Post-operative Course:

Follow-up of the other five infants from six months to over one-and one-half years has been excellent. Each maintains an oral intake which has progressed with age from liquids to pureed foods to table foods. Weight gain has been normal. None have shown evidence of dysphagia, regurgitation and none have required esophageal dilatations. The brassy cough and cry, characteristic of infants treated by end-to-end esophageal anastomosis, is also recognizable in our patients. Plain barium and cine esophagram studies obtained during the first six weeks consistently showed a widely patent anastomosis without dilatation of the proximal esophagus. Assymetric indentation of the esophagus created by the obliquity of the anastomosis is particularly obvious in views of the well-filled esophagus. (Figure 4) Peristalsis of the proximal esophagus was excellent in all patients and accompanied by good stripping activity. Peristalsis in the proximal portion of the distal esophagus was discontinuous and on occasion accompanied by reverse peristalsis. Neither stagnation of barium in the esophagus nor regurgitation into the pharynx was observed.

Discussion

Operative management of esophageal atresia by end-to-side anastomosis and ligation of the tracheo-esophageal fistula was first attempted in Europe by Sulamaa[8] in the early 1950's and later introduced in this country by Berman and Berman.[9] These authors preferred double suture ligation of the tracheo-esophageal fistula and a single layer anastomosis with #5-0 silk sutures; aside from these differences, our operation is identical to their description. Despite the good results, the initial enthusiasm for the operation waned when instances of severe post-operative coughing were reported[10] and because of concern that the ligated tracheo-esophageal fistula would eventually recanalize. Beardmore[11] and his associates re-introduced the end-to-side operation in 1966 when the problems of anastomotic stricture and esophageal dyskinesia from end-to-end

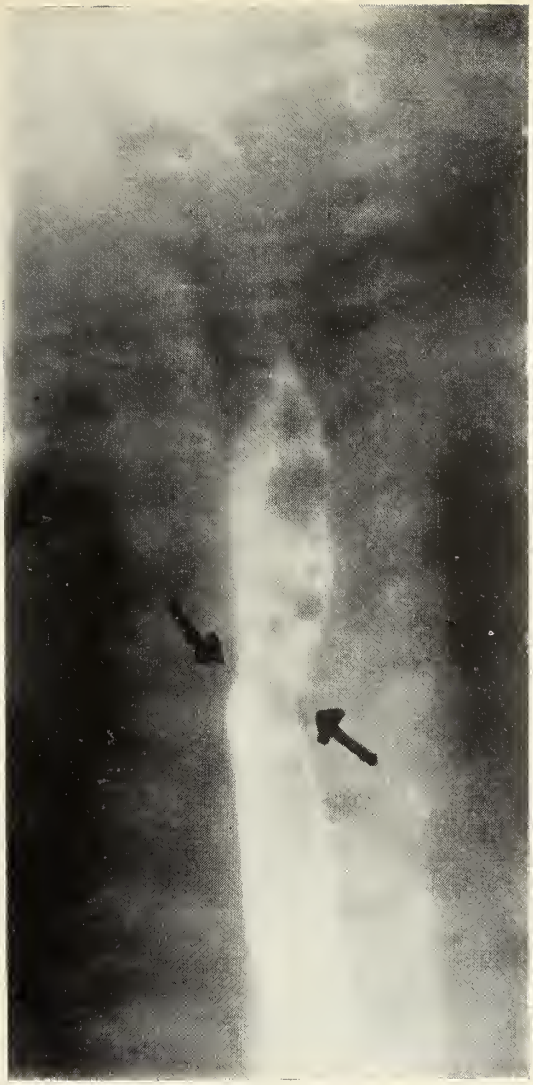


Figure 4

Esophagram six weeks following operation with asymmetric indentation created by the oblique anastomosis.

anastomosis appeared insoluble. Modifications of the technique as described by Beardmore, including single ligation of the fistula and fewer but heavier sutures for the anastomosis further lessens the risk of fistula recanalization and anastomotic complications. A total of nearly forty patients[8-11] have now been reported without a single instance of fistula recurrence or death attributable to the operation.

Although stricture of the anastomosis has not been a problem in our patients, motility of the distal esophageal segment by cine esophagram demonstrates some reverse peristalsis and inadequate stripping function. Beardmore and others have emphasized that deficient motor activity of the distal esophagus following repair often stems from injury to the branches of the vagus nerve and the arterial blood supply from the bronchial artery at the site of origin of the tracheo-esophageal fistula. Minimal dissection and careful exclusion of these structures from the ligature may eliminate this complication. Despite these abnormal radiographic findings, dysphagia has not been a clinical problem in our patients.

Some concern has been expressed about the likelihood of creating a shelf or diverticulum upon ligation of the fistula. This has not been demonstrated radiographically, although noted in the autopsy specimen. Of interest, as an incidental finding, is the asymmetric indentation of the esophagus which must not be confused with stricture. This radiographic finding is undoubtedly created by the obliquity of the anastomosis and is actually seen only upon distention of the esophagus.

End-to-side anastomosis with ligation of the fistula may be performed in premature infants, as in case number two, when there is near approximation of the esophageal segments. In most instances, however, staged operations must still be strongly considered to eliminate prolonged anesthesia and the higher risk of post-operative pulmonary complications in these tiny infants.

Summary

Anastomotic stricture and dyskinesia of the reconstructed esophagus are not uncommon when esophageal atresia is treated by end-to-end anastomosis and division of the tracheo-esophageal fistula. The technique we describe is ligation without division of the tracheo-esophageal fistula and end-to-side anastomosis of the blind upper pouch of the atretic esophagus to the superior aspect of the esophagus distal to the ligated fistula. This operation has been performed in six consecutive infants undergoing primary esophageal anastomosis since October of 1967. One infant with agenesis of the left lung expired from pulmonary complications two months following operation but all others are growing and in good health. These infants have nearly normal esophagram studies and none have required esophageal dilatation. The total current experience with this technique in nearly forty reported cases supports our finding of improved esophageal peristaltic activity and a much decreased incidence of anastomotic stricture. These results make this procedure preferrable to all others for the primary treatment of esophageal atresia with tracheo-esophageal fistula.

Discussion of Dr. Touloukian's paper: Operative Management of Esophageal Atresia.

Dr. Charles Parton: We have not had an occasion to use this very nice procedure at Hartford, but

I'm sure that we will in the future. Have your patients required postoperative dilatation or intraoperative maneuvers to elongate the proximal segment?

Dr. Richard Priebe, N.Y.C.: All of the infants in the series were over 2,000 gms. I would like to ask Dr. Touloukian if he would use this procedure in a smaller infant or would he prefer a staged operation?

Dr. Douglas Farmer: What was the status of the mucosa in the autopsy case at the site of the ligature and was the suture still on the outside of the muscularis or had it eroded through?

Dr. Robert Touloukian: In patients who have considerable disparity between the proximal esophageal and distal esophageal segment, I think it is unwise to try to stretch the proximal esophageal segment and perform an end-to-end anastomosis. In this group of six patients the esophageal segments were within a centimeter or so of each other and we had no difficulty in approximating them, but if they were further apart then I would favor a staged approach in which we divided the distal tracheal esophageal fistula and waited and then went ahead and did an end-to-end anastomosis. I would also continue to stage any premature infants because they will have a greater morbidity and mortality if we attempt to do a primary anastomosis. The suture was buried in the muscularis. The mucosa was replaced by a fibrous cord. There was a very shallow diverticulum at the site of the anastomosis and the trachea.

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An Experience With Pre-Scalene Lymph Node Biopsy and Mediastinoscopy

Joseph P. Dineen, M.D. and Jashwant Patel, M.D.

Two years ago the authors published a paper in this state medical journal outlining the historical aspects, technique, and indications for mediastinoscopy.[1] The initial report presented the experience obtained in the first 21 examinations. To date a total of 126 mediastinoscopies have been performed along with 176 pre-scalene and cervical lymph node biopsies. The results of this work are the subject of the present report.

Results

During a four year period there were 50 cervical or supraclavicular node biopsies performed in patients with palpably enlarged nodes in the neck. 42 or 84% of these biopsies were positive (Table 1). There were 126 true scalene lymph node biopsies performed on 119 patients (Table 2). Eleven or 9% of the total group were positive. Of the patients with carcinoma of the lung there were 9 positives of 92 procedures (10%). There were 19 complications in the entire group of 176 biopsies, 8 of which occured in the tumor patients undergoing true scalene lymph node biopsy (9%) (Table 3). Save for one instance of hemorrhage from a transverse cervical artery in a very uncooperative patient under local anaesthesia, none of the complications was significant.

Of the first 120 mediastinoscopies there were 69 patients with proven carcinoma of the lung (Table 4). Twenty-one or 31% of these patients had positive mediastinal biopsies for metastatic tumor, and 46 or 69% were negative to gross examination and biopsy. Of the 21 patients with secondary mediastinal involvement only five have reached thoracotomy, four of them folowing a course of radical radiotherapy. Two patients were resected post-radiation and the other three were non-resectable. None of the 21 patients has survived 8 months. Of the 46 negative examinations, 38 patients underwent thoracotomy. Thirty-one of the 38 or 82% were resectable.

TABLE 1

CERVICAL OR SUPRACLAVICULAR NODE BIOPSY

1964-1967

For diagnosis only	33		
Negative	6		
Positive	27		
		Hodgkins	3
		Lymphoma	1
		Lymphosarcoma	1
		Reticulum cell sarcoma	1
		Metastatic:	
		Larynx	1
		Nasopharynx	1
		Lung	13
		Prostate	1
		Thyroid	1
		Colon	1
		Bile ducts	1
		Glioblastoma	1
		Stomach	1
To assess operability	7		
Negative	1		
Positive	6		
		Lung	5
		Vocal cords	1
For diagnosis and operability	10		
Negative	1		
Positive	9		
		Lung	7
		Pancreas	1
		Stomach	1

		Positive
For diagnosis only	33	27
To assess operability	7	6
For diagnosis and operability	10	9
	50	42

Table 5 outlines the indications for mediastinoscopy in the total series of 126 patients. In the

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TABLE 2

TRUE SCALENE NODE BIOPSY

1964-1965-1966-1967—4 YEARS

Number of Patients	119
Number of Biopsies	126

Positive—11 (9%)

	Patients	*Procedures*	*Positive*
Diagnosis—Carcinoma	86	92	
For diagnosis	12	12	2
To assess operability	33	36	4
For diagnosis and operability	41	44	3
	86	92	9
Diagnosis—Non-tumor	33	34	
For diagnosis only	12	12	2*
Rule out carcinoma	21	22	0
	33	34	2

*Sarcoid.

TABLE 3

COMPLICATIONS—SCALENE NODE BIOPSY

Fever (101.8, 102, 101.4)		3
Hemorrhage		2
Required re-exploration wound	1	
Operative control, poor cooperation	1	
Hematoma		5
Seroma		3
Wound infection		1
Induration wound		1
Fullness wound		1
Parotitis		1
Paroxysmal auricular tachycardia		1
Grand mal seizures		1
		19

COMPLICATIONS—TRUE SCALENE (TUMOR)

Fever (101.4)	1
Hematoma wound	1
Seroma	2
Seroma wound	1
Induration	1
Fullness	1
Paroxysmal auricular tachycardia	1
	8

TABLE 4

DATA ON FIRST 120 CASES

APRIL 1966-NOV. 1969

Carcinoma Lung		
Mediastinoscopy Positive		21 (31%)
Resected post radiation	2	
Non-resectable post radiation	2	
Non-resectable	1	
Mediastinoscopy negative		46
Resectable	31 (82%)	
Unresectable	7	
No Surgery	7	
Radiation	1	

TABLE 5

126 CASES—APRIL 1966-NOV. 1969

	Examinations	*Positive*	*Percentage*
Carcinoma			
Diagnosis only	4	1	25%
Diagnosis and Assess Operability	52	15	29%
Assess Operability	19	5	26%
	75	21	28%
Diagnosis only (non-tumor)	11	6	
Rule out carcinoma	26	—	
Rule out lymphoma	4	2	50%
Carcinoma esophagus			
Diagnosis and Assess Operability	1	1	
Assess Operability	2	0	

group with carcinoma of the lung, there have been 75 examinations, 21 of which have been positive. Fifteen of the positive examinations have been patients with no previous histologic proof of carcinoma. Thus twenty per cent of the diagnoses of carcinoma of the lung were made only by mediastinoscopy prior to thoracotomy.

Table 6 records the complications associated with mediastinoscopy in the 126 cases. None has proven serious and there has been no mortality. Seventy-three of the patients have had some degree of temperature elevation post-mediastinoscopy.

Comment

Comparison of our scalene lymph node biopsy experience with mediastinoscopy indicates that in the same group of patients with carcinoma of the lung coming to final pre-treatment evaluation, having no palpable nodes in the neck, the Carlens examination (mediastinoscopy) will reveal positive mediastinal involvement in 31% and the Daniel's

TABLE 6

COMPLICATIONS

Hemorrhage		2
Pneumothorax		2
Cervical hematoma, wound		2
Wound fluctuance—gelfoam extrusion		1
Superficial wound hematoma		1
Wound infection		1
Stitch abscess		1
Hoarseness, slight		1
Fever		73
Low grade	24	
Moderate	28	
Significant	21	

COMPLICATIONS RELATED TO ANAESTHESIA

Hypotension	1
Hoarseness, difficult intubation	1
Arrhythmia	2

operation (scalene node biopsy) in 10%. This corresponds well with world-wide experience.[2] In no instance was a scalene node biopsy positive where the mediastonoscopy had been negative. Initially scalene node biopsy was performed during the course of the work-up under local anaesthesia, and mediastinoscopy reserved for the final pre-treatment evaluation if all other tests were negative. During the past two years we have combined the procedures under the same anaesthesia, often with the bronchosopy, in those patients who have no palpable neck nodes. We have continued to perform the Daniel's operation despite its low relative yield in order to completely stage the disease and help in determining prognosis.

As in most centers we now feel that a positive scalene node biopsy in patients with carcinoma of the lung, regardless of cell type, makes the patient incurable and inoperable despite radical preoperative radiation. There remains disagreement whether positive subcarinal or paratracheal nodes carry the same grim prognosis. A number of thoracic surgeons still feel that resection, perhaps with extensive enbloc node dissection, combined with supervoltage radiation can salvage many of these cases.[3] Our experience with this group of patients having positive mediastinal nodes, often microscopic with no gross involvement of the mediastinum, has given us a pessimistic outlook toward these cases. With no significant survival in the 21 positive cases and with only 5 of these patients reaching thoracotomy, we now favor utilizing X-ray therapy as the only form of treatment in this group of patients.

We continue to prefer resection alone for cure in that group of patients who are medically operable and who have no evidence of involvement either in the mediastinum or outside the ipsilateral thorax. Pneumomediastinography is now used to supplement our critical preoperative assessment by searching for mediastinal involvement outside the field of the mediastinoscope. We do not use preoperative radiation routinely in this group of patients because our operative complications following radiation have paralleled those reported by Linberg.[4]

Prior to the use of mediastinoscopy our resectability rate at thoracotomy for carcinoma of the lung was 65%. We now have an 82% resectability rate in those patients having a negative mediastinoscopy. With further experience and the addition of pneumomediastinography we hope to eliminate completely the "fruitless" exploratory thoracotomy.

Complications have been rare save for the temperature elevation noted. This has been due in all cases to difficulty in completely clearing the tracheobronchial tree of secretions in a group of patients, who in addition to their lesions, have chronic bronchitis and heavy smoking histories. There has been no instance of mediastinitis. The most potentially serious complications were the two instances of bleeding. Both were due to biopsies of lymph nodes, in one case near the azygos vein and in the other near the right pulmonary artery. Traction on the nodes caused tears in those vessels. The bleeding, amounting to approximately 200 c.c.s was immediately controlled by pressure, and the area then covered with gelfoam pledgelets. No transfusion was necessary and postoperatively the patients did well. Great care is always exercised in dissecting the nodes free of the vessels prior to biopsy, but in both cases marked adhesions were present in the area due to old inflammatory disease. The two instances of pneumothorax were of minor nature, only one receiving a small intercostal catheter for several hours. We have felt that the mortality and complication rate of mediastinoscopy have been acceptable, and have compared most favorably with that of exploratory thoracotomy to determine non-resectability.

Summary

Experience with mediastinoscopy and scalene node biopsy during the past four years reveals that mediastinoscopy has tripled the yield of positive material obtained by scalene fat pad biopsy, has partially eliminated the "fruitless" exploratory thoracotomy, and has done so without mortality and with an acceptable complication rate. It is planned to further refine this work and to supplement its usefulness with the addition of pneumomediastinography.

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Current Controversies Surrounding Major Hepatic Resections

Gerald O. Strauch, M.D.

> *. . . yet the liver is great in all men, because they have need of a great quantitie of bloud for the repair of so many spirits and the substantificke moisture, which are resolved and dissipated in every moment by action and contemplation.—Ambroise Pare*

Evolution in the conduct of major hepatic resections continues. As increasing numbers of surgeons have undertaken hepatectomies, controversies regarding several aspects of these operations have become apparent. This communication will outline some salient points of ongoing discussion, realizing that at present, personal preferences may perforce dictate practice.

At the outset is should be understood that the ultimate in hepatic resection, total hepatectomy with hepatic transplantation, is outside the realm of this discussion, except as certain problems touch both subtotal and total hepatectomy.

Our interest in major hepatectomies stems from the work of the late Dr. George Pack[1] as it related to gall bladder carcinoma.[2] Recent experiences have magnified that interest.

Case Reports

Case I. No. 536511. A 34-year-old Negro man underwent emergency operation on October 3, 1968, because of apparent massive intra-abdominal hemorrhage following his involvement in an automobile accident several hours prior. A ruptured spleen was removed, and a ten centimeter laceration of the left hepatic lobe's lateral segment was sutured. His post-operative course was uncomplicated, and he was discharged on his fifteenth post-operative day.

He was re-admitted on November 8, 1968 because of epigastric pain and a large epigastric mass extending into the left upper abdomen. Modest anemia and leukocytosis were present; liver function studies were normal. Barium studies of the upper gastrointestinal tract revealed displacement of the gastric lesser curvature to the left and posteriorly. A clinical diagnosis of post-traumatic intraparenchymal hepatic hematoma seemed clear. Operation on November 10, 1968, confirmed a huge hematoma, involving the entire left hepatic lobe, which had ruptured into the left subphrenic space. Total left hepatic lobectomy and gastrostomy were performed. His post-operative course was marred by pulmonary atelectasis and wound infection, but he was discharged on his twentieth post-operative day and has remained well.

Case II. No. 538496. A two-year-old white male was discovered to have a massive right upper abdominal tumor after he was hospitalized for a fractured left femur sustained in a fall on ice on January 4, 1969. Detailed diagnostic studies were completed within seventy-two hours after surgical consultation was requested and failed to reveal a renal tumor or evidence of systemic metastases. Laparotomy disclosed a right lobar liver carcinoma of mixed cell type without evidence of left lobar involvement or metastases. Total right hepatic lobectomy and gastrostomy were carried out. His recovery was without incident, and treatment for his femoral fracture was continued. Follow-up chest films four months after operation demonstrated bilateral pulmonary metastases. The child remains under treatment with chemotherapeutic agents at this time.

Discussion

Indications

The indications for major hepatic resection do not merit extended discussion here. Trauma and neoplasm remain the chief indications,[3-5] though rarer problems present themselves. It can be said with assurance that in most settings more patients are suffering today from an omitted but indicated hepatectomy than from a non-indicated extirpation of a diseased hepatic segment or lobe; the experience with battle casualties in Viet Nam, however, may prove an exception to this statement.[6] Since primary hepatoma is currently unrewarding as an application for hepatic transplantation,[7] an aggressive approach to subtotal hepatectomy seems justified in patients so afflicted. Conversely, diffuse cirrhosis has become a contraindication to subtotal hepatectomy, but a process viewed with increasing enthusiasm by the "transplant surgeon."[7] Carcinoma of the gall bladder cannot realistically be claimed as an indication for major hepatectomy today, as Brasfield's single case, reported in 1961,[8] remains the only five-year cure following "extended right lobectomy" of which we are aware.

Pre-Operative Studies

The pre-operative evaluation of the patient who may be a candidate for hepatic resection likewise cannot be said to arouse much true controversy; rather, a plea is made for the recognition of diagnostic options by the surgeon so that precision and

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efficiency in diagnosis are obtained. Such options will vary largely on the basis of the emergent or elective nature of the surgical problem.

Types of Resection

Although papers appear alluding to segmental surgical liver disease,[9] and although hepatic subsegments or "areas" are also anatomically defined,[10] the number of cases involving true anatomic planes of resection other than those of the interlobar or left intersegmental planes are few indeed. Further, one can predict that such will remain the case in view of hepatic anatomy and the problems for which hepatic resection is appropriate.

Technic

Several points in the technic of hepatectomy have engendered discussion over and above the minor technical variations noted from one surgeon to another.

The use of hypothermia has not attained general acceptance for very practical reasons. While hepatic inflow occlusion can unquestionably be safely extended for substantial time periods with a hypothermic patient, the technic is too cumbersome for emergency problems, and total hepatic inflow occlusion is not often required in elective cases. Hemorrhage as a major problem during hepatectomy will in most instances have a hepatic venous origin, and hypothermia will be of little strategic value. Most authors have not felt that hypothermia adds enough advantage to justify its incorporation as standard procedure in hepatectomy.

In the securing of the hepatic veins during elective resection, some prefer hepatic venous indentification and ligation prior to hepatic parenchymal division.[11, 12] We agree with those who elect to secure the hepatic veins following hepatic division,[13, 14] as it seems easier and safer; we have not used the technic of intermittent suprahepatic vena caval obstruction described by Gentile and MacLean[15] to identify the hepatic veins. The problem of hepatic venous control following traumatic avulsion of the veins themselves may be solved more often than formerly by the use of Schrock's internal atriocaval shunt.[16]

Attempts to control continued slow hemorrhage from the raw liver surface following resection have included the use of omentum,[14] falciform ligament,[14] Glisson's capsular remnants,[13] split-thickness skin grafts,[14] manufactured hemostatic products,[3] various suture technics,[12, 14, 17] and, more recently, cyanoacrylate resins.[18] We are impressed that proper anatomic liver resection should not require such maneuvers normally, that covering the raw surface may lead to undesirable accumulations of blood and bile, and that the best management of the raw surface following meticulous control of discrete vessels is by generous sump drainage of the resection area.

Biliary tract drainage following major hepatectomy has received varying support since Merendino's advocacy of this adjunct in 1963.[19] Whereas cholangiography, during or after operation, may serve as an invaluable tool when complications arise, especially following resection for traumatic liver injury,[6] the benefits of "hepatic decompression" have proved more theoretical than real;[3, 20] in fact, the production of hepatic decompression by external biliary drainage seems to be a myth.[21] In addition, drainage of children's tiny ducts may be fraught with some hazard.[4] It would appear that biliary tract drainage should be reserved for certain problem cases, rather than regarded as "routine."

Post-Operative Management

In general, the support of the patient following hepatic resection has proved less complicated than was once anticipated. The work of McDermott and his associates[22] established the importance of adequate albumin and glucose administration during the early post-operative period, and most other management problems encountered have not been peculiar to hepatectomies. Acute peptic ulceration has been a problem in some reported series,[3, 23] and the mechanism for it remains problematic; in this setting, there may be a specific consequence of hepatectomy playing a major role.[3]

Post-Resectional Hyperplasia

The nature of hepatic "regeneration" remains of great interest and concern. It is generally agreed that post-resectional hyperplasia, rather than true regeneration, is involved. This hyperplasia seems to be limited to hepatic parenchyma without angioneogenesis.[24] Conflicting reports exist regarding the effect of variations in hepatic blood flow on the hyperplastic process.[25, 26] Evidence is building that a humoral factor carried by portal blood may control the potency and extent of the liver's reconstitution of cell mass.[27-30] This factor apparently requires a normal hepatic remnant for fulfillment of activity, since the cirrhotic liver is incapable of post-resectional hyperplasia,[31] and since cirrhotic rats fail to demonstrate the humoral factor which seems to stimulate hepatic hyperplasia following hepatectomy in normal rats.[32] The time required for restitution of hepatic mass seems to be much more variable than formerly thought. Siemsen, studying post-resection liver scans, has noted normal hepatic size as early as one week following lobectomy.[33] The vigor of the process appears directly proportional to the quality of the hepatic remnant and inversely proportional to the equivalent of normal liver removed.

Conclusion

We have attempted to touch on some of the main areas of controversy in this young surgical territory. That these disagreements exist testifies to the place already attained by modern hepatic resection since its advent less than two deades ago.

Discussion of Dr. Strauch's paper: Current Controversies Surrounding Major Hepatic Resections.

Dr. William Livingston: Would Dr. Strauch elaborate further on postoperative T-tube drainage as an effective mechanism for decompression of the liver.

Dr. Gerald Strauch: This question of biliary drainage following major liver resection has been a provocative one since Dr. Merendino first suggested it. John Foster at Vanderbilt and Longmire in Los Angeles have questioned it very seriously, while the Ann Arbor group supports it very strongly. A recent paper by Pilcher on the Vietnam injuries questioned it again strongly. Finally, at the 1969 Surgical Forum of the American College of Surgeons in October the Wayne State Group reported a study in dogs where they produced standard hepatic injury. Intrahepatic pressures were measured by percutaneous techniques, and bile duct and gall bladder pressures were also monitored. There was no significant difference in postoperative morbidity or in intrahepatic pressure measurements between animals with bile duct drainage, gall bladder drainage or no drainage at all.

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Careers in Health and Medical Care

With the new academic year the CSMS staff has received numerous inquiries from high school students concerning careers in health and medical care. Additional inquiries have come from physicians who have made themselves available to local guidance directors for counseling sessions.

The Society does maintain a limited number of films which could be used for high school career days or by civic, church or school organizations planning vocational guidance programs. Films may be requested through Leonard R. Tomat, Assistant Executive Director for Educational and Scientific Activities. Films include: "Career: Medical Technologist"; "Health Careers"; "Helping Hands for Julie".

Through the AMA Film Library in Chicago, the Society can make available a number of more recently produced 16 mm films. These include a twenty-eight minute colored film entitled "Horizons Unlimited" which vividly highlights the two hundred productive careers in medicine and allied fields.

A handy reference booklet entitled "A Medical Careers Handbook" is available upon request from the CSMS office in New Haven.

Femoral-Tibial Bypass: Salvage of Ischemic Lower Extremities with Inadequate Popliteal Runoff

John E. Fenn, M.D. and Donald B. Alderman, M.D.

Bypass graft with autogenous vein from the femoral to popliteal arteries in the treatment of arterial occlusive disease of the lower extremity has become a widely used and recognized procedure since it was first described by Kunlin in 1951.[1] Until recently, arteriographic demonstration of advanced atheromatous disease in the popliteal artery or the absence of "runoff" from this artery precluded a reconstructive approach and surgeons were reluctant to attempt salvage of a limb under such circumstances because of the high failure rate. In 1961 McCaughan[2] reported successful anastomosis to the tibial arteries in the upper third of the leg. Since then, others[3, 4] have reported larger series with anastomoses to the more distal tibial vessels including the anterior tibial artery at the ankle.[5]

Eight patients who, on the basis of their arteriograms, would not have been considered for bypass graft a few years ago have undergone femoral-tibial bypass and are reported here.

Clinical Material

Eight distal tibial artery bypasses were performed in the 11 month period between November, 1968, and October, 1969. There were seven men and one woman between 46 and 77 years of age (Table 1). Five patients had diabetes mellitus and all had been well controlled with either insulin or an oral hypoglycemic agent until the onset of their ischemia except for one patient whose diabetes was discovered at the time of his preoperative workup. All of the patients had rest pain and six of the eight had already developed localized gangrene or necrosis.

Two patients had previously undergone femoral-popliteal bypass grafts which had failed probably because of progressive atherosclerotic disease in the popliteal artery. Lumbar sympathectomy was either combined with femoral-tibial bypass or had been done previously in three patients.

TABLE 1

AGE AND SEX DISTRIBUTION

7 MALES, 1 FEMALE

Ages	*Ages*
40-49 — 1	60-69 — 1
50-59 — 2	70-79 — 4

The operation done most frequently (5 patients) was an autogenous vein bypass from the common femoral artery to the posterior tibial artery just above the medial malleolus. Two patients had bypasses to the anterior tibial artery and one to the dorsalis pedis. The common femoral artery was the preferred site for takeoff of the bypass graft but when the vein graft was not long enough to reach the full distance, the superficial femoral artery was used provided it was soft and relatively free of disease. In that two patients had previously had femoral-popliteal bypasses it was necessary to use their contralateral autogenous saphenous veins for the femoral-tibial bypass.

In every instance distal tibial patency was demonstrated by preoperative arteriography and it was primarily on this basis that patients with advanced ischemia were selected for operation.

The following selected cases are representative of this series;

Case Histories

Case 1. L. H., a 56 year old white male, was first seen on 2/18/69 with a two month history of a cyanotic painful right great toe. One month previously he had developed small painful ulcerations along the lateral aspect of his left ankle. He had long had cardiac disease with known auricular fibrillation. He had sustained a massive cerebrovascular accident six years before and was left with a residual right hemiparesis. His speech had been unaffected and he was able to carry on relatively normal activity as a shopowner until the rest pain in his right foot and ankle had incapacitated him. There was no history of diabetes mellitus.

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On examination, the left femoral, popliteal, and dorsalis pedis pulses were intact. No pulses could be felt below the right common femoral artery. There were two ulcers which measured one centimeter in diameter just anterior to the lateral malleolus. The right great toe was cyanotic and tender.

A femoral arteriogram confirmed the right superficial femoral artery occlusion but the popliteal artery did not reconstitute. The anterior tibial and peroneal arteries opacified briefly but only the posterior tibial artery appeared patent as far as the malleolus.

On 2/25/69 a common femoral to posterior tibial artery bypass was carried out using the reversed ipsilateral long saphenous vein as an arterial substitute. The posterior tibial pulse behind the medial malleolus was palpable on the operating table and has remained strong to the present time. The rest pain promptly abated and the ulcers healed. Repeat femoral arteriography performed 10 days postoperatively confirmed patency of the graft.

Case 2. M. B., a 77 year old white female diabetic presented because of severe rest pain in her right foot and a painful ischemic ulcer over the head of her first metatarsal. She also had had moderate hypertension for many years but there was no other cardiac or renal disease history.

On examination, the left femoral, popliteal, and dorsalis pedis pulses were present. The right femoral pulse was also present but the right popliteal pulse was markedly reduced in intensity although present. No pulses could be felt below this point in the right leg. A tender two centimeter ulcer was present along the medial aspect of the right foot over the head of the first metatarsal.

A femoral arteriogram disclosed advanced atherosclerotic disease of the right superficial femoral artery but without complete occlusion. The anterior and posterior tibial arteries were both obstructed shortly after their takeoff, but the anterior tibial artery reconstituted just proximal to the dorsalis pedis.

On 7/25/69, a common femoral-dorsalis pedis bypass was carried out using the reversed ipsilateral long saphenous vein as a graft. A strong pulse was immediately palpable in the subcutaneous graft and by the evening of surgery a pulse could easily be felt in the distal dorsalis pedis. The foot immediately became warm and pink.

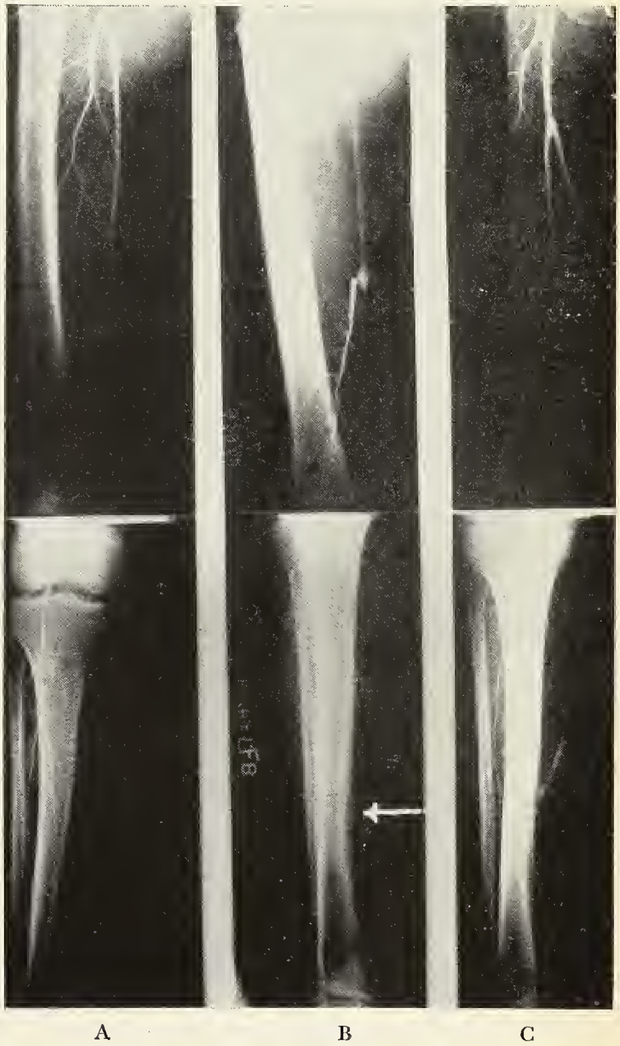
On the fourth postoperative day, pulmonary edema suddenly developed and an electrocardiogram showed an acute myocardial infarction. The pulmonary edema was successfully controlled and it was elected to begin heparin therapy at this point. By the next day a hematoma had developed under the skin flaps of the distal incision on the dorsum of the foot and in spite of evacuation of this hematoma, the skin flaps remained cyanotic and eventually underwent necrosis which exposed the distal anastomosis into the dorsalis pedis. The distal dorsalis pedis pulse disappeared but the vein graft pulse remained strong. Recovery from her myocardial infarction was satisfactory and she was seen thereafter weekly as an outpatient for debridement of the ulcer on the dorsum of her foot. The vein graft pulse remained strong and as the wound granulated vigorously there was no further rest pain.

Three months postoperatively she awakened to find active arterial hemorrhage from the base of the residual ulcer and examination in the emergency room disclosed a false aneurysm at the distal anastomosis with rupture. The vein graft was ligated just in front of the fibular head under local anesthesia in order to control the hemorrhage. Within a week severe rest pain had recurred with rapid progressive necrosis of the dorsum of the foot. She became febrile and toxic with rapid spread of the ischemia centrally and above knee amputation was carried out on 11/13/69, 3½ months following her bypass.

Case 3. A. O., a 53 year old white male diabetic was seen on 7/5/69 because of ischemic rest pain in his foot which had become severe during the preceding three days. An inferior myocardial infraction had occurred three years before.

Examination showed a pale, cool right foot which was strikingly moist. No pulse was present below the right common femoral and the superficial femoral artery block was confirmed by femoral arteriogram which also showed a patent but moderately diseased popliteal artery (Fig. 1A). A standard femoral-popliteal bypass graft using reversed ipsilateral autogenous vein was done on 7/9/69 and a right

Figure 1



(Case 3) A. Femoral arteriogram showing right superficial femoral artery occlusion and diseased but patent popliteal artery. Patient underwent femoral-popliteal bypass. B. After failure of femoral-popliteal graft, arteriography no longer shows popliteal artery but posterior tibial is open (arrow). C. Patent superficial femoral-posterior tibial graft.

lumbar sympathectomy was also performed at the same time. The immediate symptomatic result was good and the patient regained a strong posterior tibial pulse.

Two months postoperatively at a routine office visit, the posterior tibial pulse was found to be absent and the foot was again cool and pale. The patient reported that this had occurred quite suddenly four days before and that rest pain had recurred.

Readmission was arranged and a second femoral arteriogram confirmed non-patency of the graft and no visualization of the popliteal artery (Fig. 1B). The posterior tibial artery reconstituted distally and on 10/3/69, a proximal superficial femoral-posterior tibial graft using reversed contralateral saphenous vein as an arterial substitute was performed with restoration of the posterior tibial pulse and relief of symptoms. The superficial, rather than the common femoral artery, was used for proximal anastomosis in this patient in that the vein graft was not of sufficient length to reach the common femoral. A repeat femoral arteriogram was done 10 days postoperatively and showed patency of the femoral-tibial graft (Fig. 1C).

Operative Technic

After general anesthesia has been administered and with the patient in the supine position, both legs and the abdomen are prepared and draped. Lumbar sympathectomy, when indicated, is carried out first. The distal tibial artery is exposed to assess its suitability for subsequent anastomosis. The posterior tibial artery is exposed approximately 10 centimeters above the medial malleolus as it lies between the flexor hallucis longus and flexor digitorum longus muscles. Great care is exercised in this portion of the dissection to gently tease the artery away from the companion veins. It is usually necessary to divide or loop a few of the many small branches of the artery. When the anterior tibial artery is to be used rather than the posterior, it is exposed at the same level and lies just in front of the interosseous membrane between the extensor hallucis and tibialis anterior muscles. If the arterial wall is soft and the artery collapsible, a cotton pledget soaked in one per cent procaine is placed on the artery and a moistened sponge packed loosely in the wound. In our experience, the outside diameter of the artery has not been more than two millimeters and we have been able to work successfully with one posterior tibial artery that measured only one millimeter.

The long saphenous vein is then removed from its termination in the common femoral vein to just above the medial malleolus through multiple separate incisions along the medial thigh and leg. If the posterior tibial artery is to be used for distal anastomosis, this same subcutaneous tunnel created for removal of the vein is used to house the reversed vein as an arterial substitute. A separate subcutaneous tunnel is required when the anterior tibial artery (or dorsalis pedis) is to be used and this is created by blunt means from the proposed point of proximal anastomosis to the antero-lateral part of the leg by crossing to the lateral thigh at mid-thigh level in order that the tibia may be avoided (Fig. 2). It is convenient to place the tunnel just in front of the fibular head and the common peroneal nerve is not endangered if the dissection remains strictly subcutaneous.

The various branches of the saphenous vein graft are ligated with 3-0 silk and the venous adventitial debris stripped. Particular attention is directed to any cicatrical bands and once these have been disrupted the vein is distended and flushed with heparinized saline (1000 units of heparin per 100 cc. of saline). As preparation of the vein graft is completed the patient is systemically heparinized with 5000 units of heparin intravenously and then 2500 units of heparin given directly into the common femoral artery. The distal tibial artery is controlled by means of 2-0 silk loops drawn through

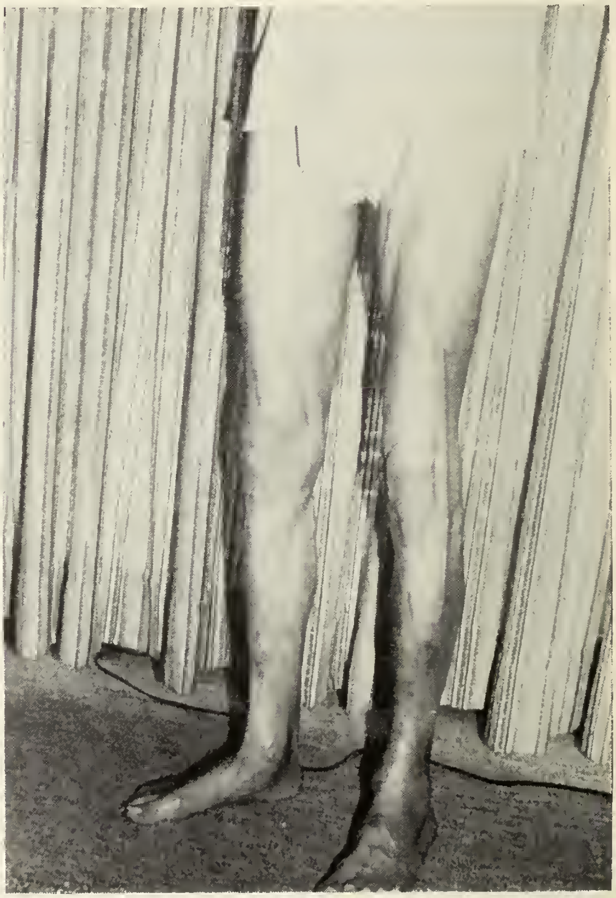


Figure 2

Subcutaneous course of autogenous vein bypass graft between left common femoral and left anterior tibial arteries.

polyethylene tubing to act as snares. This arrangement has produced little trauma to the delicate tibial arteries. A one centimeter longitudinal arteriotomy is carefully made in the tibial artery and a few cubic centimeters of heparinized saline are injected into the distal artery through the arteriotomy by means of a fine polyethylene cannula.

The central end of the saphenous vein graft is appropriately fish-mouthed and the corners are not trimmed until a portion of the anastomosis has been completed so that they may be used as holders. The distal anastomosis is constructed first so that the vein may be manipulated more easily during this portion of the procedure and this anastomosis tested before the proximal anastomosis is begun. Meticulous care has been used in the performance of the distal anastomosis but magnifying loops or other special optical equipment has not been necessary. Running over-and-over technic with 6-0 or 7-0 suture material has been satisfactory, but it must be recognized that placement of the distal corner suture ultimately determines the effective size of the runoff lumen.

Upon completion of the distal anastomosis the vein graft is again distended gently with heparinized saline and any significant leaks in the suture lines repaired at this time. The vein graft is then carefully oriented to avoid twisting and is drawn through the subcutaneous tunnel. A vertical arteriotomy may be used in the femoral artery when the vein graft terminates in the posterior tibial artery, but for the anterior tibial bypasses, an oblique arteriotomy is preferable so that the vein graft can cross the anterior thigh without acutely angulating just beyond the femoral anastomosis. Running over-and-over technic is also used for the proximal anastomosis with 5-0 or 6-0 suture material. The common femoral artery is preferred for proximal anastomosis, but when the vein graft will not reach, a soft and strongly pulsatile superficial femoral artery serves well. Limited superficial femoral endarterectomy has not been required in this series of patients, but this would appear to be the procedure of choice if the vein graft is too short and the superficial femoral artery is highly diseased.

The usual flushing maneuvers are employed to avoid the embolization of particulate matter into the distal tibial arteries. Systemic heparin, which is administered intravenously in 5000 unit increments hourly does not always require neutralization with protamine sulfate. Low molecular weight dextran is begun in the operating room on all patients and is continued for the first four post-operative days. Antibiotics are not used routinely.

Results

Within 24 hours of operation all eight patients regained either the posterior tibial or dorsalis pedis pulse with abolition of rest pain. There have been no late spontaneous failures. Two patients have now had functioning grafts for one year. Five of the six patients with patent grafts are more than six months postoperative.

One non-diabetic patient who had previously undergone an unsuccessful femoral-popliteal vein graft occluded his femoral-posterior tibial graft on the fourth postoperative day. The cause for this single spontaneous failure was felt to be the presence of significant atherosclerotic disease in the posterior tibial artery at and beyond the site of anastomosis, A below the knee amputation was later carried out because of progressive rest pain and necrosis. One other patient, already reviewed in this report, developed an infection in her graft at the dorsalis pedis anastomosis and the graft was ligated in order to control hemorrhage. An above the knee amputation was subsequently required.

Of the remaining six patients with patent grafts, one required a local amputation of two toes which healed primarily. Three other patients healed localized areas of necrosis or gangrene spontaneously within a month of operation.

In addition to the single graft failure in the early postoperative period, there were two other significant complications: One patient with a femoral-anterior tibial graft developed a hematoma in the anterior thigh which was evacuated. The diabetic patient who had undergone femoral-dorsalis pedis bypass sustained a myocardial infarction on her fourth postoperative day. Treatment of this complication with heparin probably contributed to the breakdown of her distal wound and eventual graft infection which resulted in graft ligation for control of hemorrhage.

Postoperative ankle edema was common in many patients but consistently resolved rapidly with elevation of the extremity and did not persist longer than a few months.

There were no deaths.

Four of the five diabetics in this series continue to have functioning grafts and all are free of symptoms.

Discussion

Patients were selected for operation on the basis of their symptoms, findings, and arteriography. No patient with claudication alone was considered to be a candidate for operation and all patients had either rest pain or tissue breakdown with gangrene or necrosis. As we gain more experience with this procedure, it is our feeling that patients with incapacitating claudication should also be considered for operation. Until now, all femoral-tibial bypasses were done on patients whose limbs were doomed to amputation.

The single diagnostic study which determined feasibility of reconstruction was the arteriogram. In view of the successes reported here and by others,[3, 4] it is essential that femoral arteriography be planned so that possible opacification of the tibial vessels at the ankle can be seen. We make a point of getting at least the proximal portion of the foot on the X-ray film and time the study so that the most distal portion of the tibials can be seen. The site and length of the block are of less importance and can be determined largely on clinical grounds. Patients who demonstrate highly diseased popliteal arteries with relatively normal-appearing tibial vessels below should be considered for femoral-tibial rather than femoral-popliteal bypass. The majority of arteriograms done in the group of patients reported here failed to show any opacification of the popliteal artery whatever, but it is our feeling that advanced disease of the popliteal artery is a common cause for failure of femoral-popliteal grafts, and is an indication for femoral-tibial graft if the tibial arteries appear in better condition.

When there is a choice between the anterior and the posterior tibial arteries for distal anastomosis, the latter is to be preferred because the same tunnel created to dissect the vein can be used to contain the graft. While placement of the grafts in a subcutaneous position potentially subjects them to somewhat more risk from trauma than are the subfascial grafts, the more superficial location has some very definite advantages. During the first 24 hours, when it may be difficult to palpate distal pulses, it is convenient and reassuring to be able to palpate the subcutaneous graft. On the occasions when we have not reversed the intraoperative heparin with protamine, we have done so with the knowledge that even a very small hemorrhage would not escape detection for long and the heparin could be counteracted promptly. Finally, it has provided a convenient and simple monitor for the patient to assess his own status after his hospital discharge and to be reassured of satisfactory function.

There was some concern initially that running such a long graft from the common femoral artery to the distal tibial artery would leave a fairly large section of leg and lower thigh subject to ischemia, but, in fact, there is considerable retrograde flow into the patent tibial. One patient whose distal anastomosis was to the posterior tibial also regained his dorsalis pedis pulse, perhaps by retrograde flow around his popliteal trifurcation.

On the basis of the success with distal tibial anastomosis we believe that certain concepts in the management of arterial occlusive disease of the lower extremities should be revised. Simple visualization of the popliteal area on femoral arteriography must be considered inadequate in that such study should include the distal leg and ankle to search for patent tibial vessels. The presence of a popliteal pulse in the face of peripheral ischemia does not eliminate the possibility of reconstruction and arteriography should still be performed.

Summary

Eight patients have undergone autogenous vein bypass graft from the femoral artery to the distal tibial arteries, or, as in one patient, to the dorsalis pedis artery.

Six of the eight grafts are currently patent and there have been no late spontaneous graft occlusions.

In patients with severe arterial insufficiency of their lower extremities, arteriography showing disease-free tibial arteries with severely atheromatous or non-patent popliteal arteries has been the primary criterion for femoral-tibial bypass.

Anastomosis to the distal tibial arteries is to be preferred in the presence of a highly diseased popliteal artery;

Patients with ischemic lower extremities who previously faced amputation may have their limbs salvaged by means of anastomosis to the distal tibial or dorsalis pedis arteries.

Discussion of Dr. Fenn's paper: Femoral-tibial Bypass: Salvage of Ischemic Lower Extremities with Inadequate Popliteal Runoff.

Dr. Charles Bucknam: I wonder if the unusual course of this graft over the anterior thigh to the lateral surface of the leg does not explain some of the difficulty in keeping the grafts patent. We have done a few bypasses to arteries in the distal leg and ankle with mixed success. Do you have problems obtaining a saphenous graft of sufficient length to reach the ankle or foot?

Dr. Robert Boltax: Was there any correlation between the return of distal pulses and the relief of symptoms?

Dr. John Fenn: We haven't faced graft failure as a consequence of the lateral rerouting course yet. We have had these people do deep knee bends in our office to see if there would be any kinking, and there was not. We find if we cross the thigh at mid-thigh level and stay in front of the head of the fibula that these grafts do quite nicely. One has to be cautious about the course of the common peroneal nerve, but otherwise I think it is a fairly safe place for the graft to be. As far as the vein dissection is concerned, surprisingly enough the smallest part of these veins tends to be in the region of the knee and not in the distal area. One can dissect the saphenous vein down below the medial malleolus into the foot where it is still large enough to be useful. As an alternative solution, we have used the cephalic vein from the arm in a number of patients with good success. One can also do a superficial femoral endarterectomy and reconstruct using a graft take-off somewhat lower on the superficial femoral artery.

All of these patients regained their distal pulses within twelve hours of operation, and the patients who have patent grafts still have their distal pulses. They all lost their rest pain within 24 hours of operation.

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"ARTHRITIS"—Direct and informative this pamphlet touches upon the wide scope of this disorder and its many related illnesses.

Requests for copies of these publications should be addressed to Leonard R. Tomat, Assistant Director for Educational and Scientific Activities, 160 St. Ronan Street, New Haven 06511.

Misplaced Central Venous Pressure Catheters

Robert T. Schweizer, M.D. and James H. Foster, M.D.

The principal of central venous pressure (CVP) monitoring is very useful in the management of certain fluid replacement problems, and in the diagnosis and therapy of shock. The technique has been well described[1, 2] and consists of the pressure measurements from a plastic catheter placed in a large intrathoracic vein or in the right atrium. Several methods of locating the catheter tip have been described: electrocardiographic changes seen when the catheter enters the right atrium;[3, 4] changes in pressure levels in an attached manometer as the catheter is advanced;[1] and localization of the catheter by X-ray.[1] An estimation of the length of catheter needed to have the tip located near the heart is often sufficient when the catheter is introduced *via* the external jugular or subclavian vein. However, when introduced *via* the basilic or brachial vein, estimation of required length may be incorrect and give misleading information. We have seen catheters coil in the right atrium, enter the inferior vena cava, hepatic veins, right ventricle, curl back into the same vessel of insertion, and on over twenty occasions, catheters have entered internal jugular veins. Another complication of CVP catheters is the rare perforation of a vein[5] or the heart.[6] We had one catheter perforate the left innominate vein.

Case Reports

Case 1. A 56-year-old woman was admitted with an acute episode of hematemesis and shock. A large polyethylene catheter was placed in the right basilic vein *via* surgical cutdown and advanced to a distance judged to be near the right atrium. The fluid level in the manometer showed only slight variations with respiration, but demonstrated the small fluctuations which are due to heart beat. Abnormally high readings were obtained, in spite of brisk gastric hemorrhage, and the patient was thought to be in congestive failure. However, it was noted that the CVP readings varied with the level of the patient's head. Since the catheter was not radiopaque, it was filled with 50 percent diatrizoate (*Hypaque*) and a portable chest X-ray was obtained in order to locate the catheter tip. The X-ray showed that the catheter had entered the internal jugular vein (Figure 1). The catheter was withdrawn several inches and functioned properly, but the patient expired before adequate volume replacement or surgery could be performed.

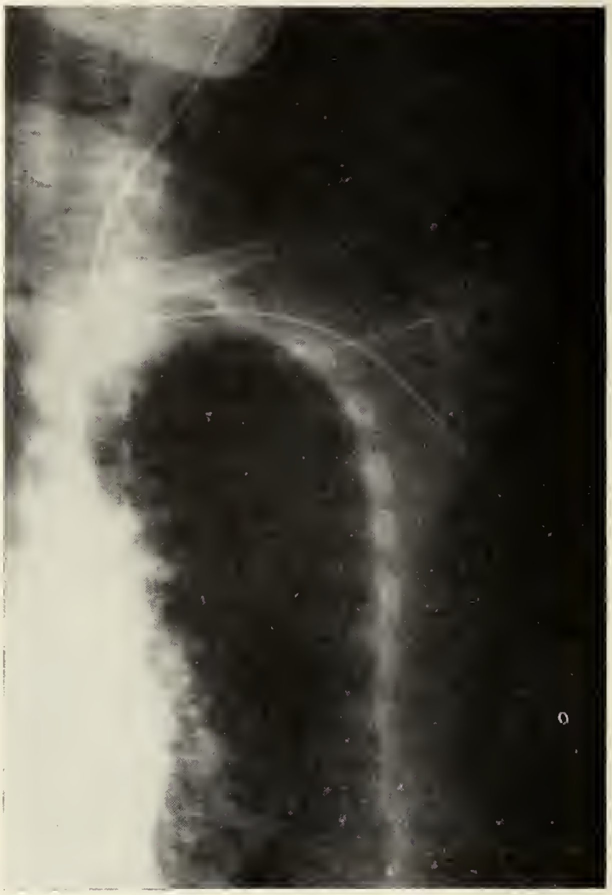

Figure 1

CVP catheter inserted *via* basilic vein entering internal jugular vein.

Case 2. An 88-year-old male was admitted with the diagnoses of septic shock from a chronic urinary tract infection, and upper gastrointestinal bleeding. To aid fluid management, a polyethylene, non-radiopaque catheter was inserted in the left basilic vein by cutdown. The surgeon reported "difficulty" in advancing the catheter. Normal fluctuation of the fluid level was seen with respiration, intravenous fluids ran easily, and pressure readings in a normal range were obtained. However blood samples could not be drawn from the catheter and the patient did not respond to therapy. He became more dehydrated and had no diuresis after a mannitol infusion. A repeat X-ray 48 hours after admission showed a widened mediastinum and a left pleural effusion. A perforation of the CVP catheter was suspected and a second radiopaque catheter was placed *via* the right arm. An X-ray was then taken with an injection of 50 percent diatrizoate in the left arm catheter. The dye was seen flowing into the mediastinum (Figure 2). CVP measurements in the new catheter were the same as those in the first catheter. After adequate fluid administration, urine output

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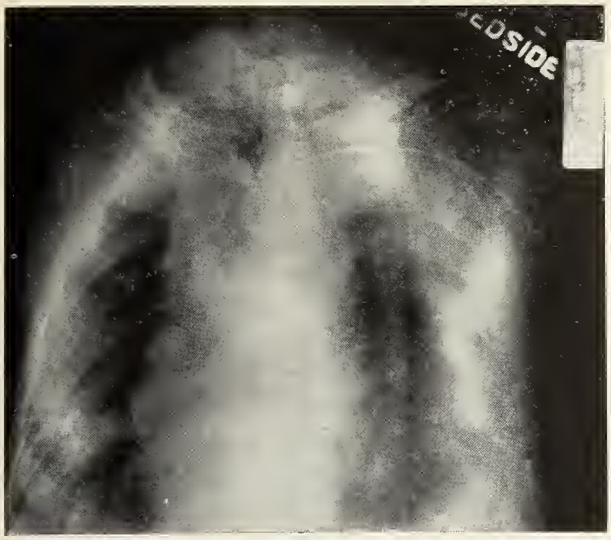

Figure 2

Perforation of left innominate vein by CVP catheter. Note contrast dye entering mediastinum.

increased and the patient improved. No further complications from the extravasation developed. The catheter tip was noted to have a sharp bevel.

Case 3. A 65-year-old woman was admitted to the Intensive Care Unit after extensive abdominal surgery. A CVP catheter was placed *via* cutdown on the right basilic vein and advanced to a position judged to be about the distance to the right atrium. Pressure readings were high at 19 centimeters of saline, and wide fluctuations in the fluid level were observed. Several minutes after insertion the patient's cardiac monitor showed multiple premature ventricular contractions and short runs of ventricular tachycardia. Intravenous lidocaine (*Xylocaine*) was administered but did not effect the arrhythmia. The CVP catheter was then withdrawn a few inches and the arrhythmia stopped. The CVP reading was subsequently in a normal range.

Discussion

Central venous pressure catheters which are not truly central in location pose a threat to successful therapy. In the cases reported, and in several other cases we have recently seen, the clinical management was compromised by the faulty information resulting from the misplaced catheters. Most of these misplaced catheters have entered internal jugular veins, and this is not surprising since catheters are often seen entering internal jugular veins during cardiac catheterization. There are two valves in an internal jugular vein[7] and variations in pressures are seen when the catheters are in these positions as compared to those in central locations. While variations due to head elevation can easily be eliminated, peripherally located catheters do not give the reliable information desired of centrally located catheters.[2]

Case 3 is typical of catheters introduced into the right ventricle, although the arrhythmias are not always observed. The position may have been suspected from the elevated pressure, and also by observing the wide fluid level fluctuations which are synchronous with the heart beat. Catheters in the superior vena cava or right atrium have their widest pressure fluctuations synchronous with respirations, and very small secondary fluctuations due to heart beat. If the catheter is withdrawn slowly with the fluid column open to the manometer as it is withdrawn, a sudden drop to lower pressures is usually seen when the tip enters the right atrium. This change may be used as a method of catheter tip location.[1]

Since CVP catheters in right ventricles yield higher pressures, they thus may mislead therapy. They may also enter the ventricle intermittently, being ejected into the pulmonary artery or flipping back into the right atrium, and thus sudden and sometimes transient changes in pressure readings may be seen. The ventricular arrhythmias which are occasionally seen are potentially lethal.

Several precautions should be taken when CVP catheters are inserted *via* veins in the arms. Entrance of catheters into the jugular veins may often be prevented by having the patient's head externally rotated and flexed toward the side from which the catheter is being introduced.[8] Catheters should never be forced when they meet resistance to passage. Rather, they should be withdrawn slightly and then readvanced slowly with a twisting motion. Easy back flow of blood should be obtained. If this does not occur, the catheter should be withdrawn slightly as it may be abutting against the vein wall at a bend in the vessel. This interferes with pressure readings and may predispose to perforation. It is not necessary to sharply bevel the catheter tip.

While many CVP catheters inserted *via* the arms may be properly positioned by the techniques mentioned, we believe that the position of the catheter tip should usually be located by X-ray to insure reliable readings. This is facilitated by the use of radiopaque catheters. Shorter catheters inserted by the external jugular or subclavian veins are usually in satisfactory position, although we have seen one catheter from the latter route enter an internal jugular vein.

Summary

Central venous pressure catheters often enter internal jugular veins or are in other ways misplaced. Such misplaced catheters may yield falsely high pressure readings and seriously alter therapy. Their

central position should be confirmed by X-ray when they are inserted from arm veins. External rotation and flexion of the head toward the arm of catheter insertion may prevent internal jugular vein cannulation.

One case of innominate vein perforation is reported. CVP catheters should never be forcefully inserted and sharp beveling of the tip is unnecessary.

Generic and Trade Names of Drugs

Diatrizoate sodium—*Hypaque*

Lidocaine—*Xylocaine Hydrochloride*

Discussion of Dr. Schweizer's talk: Misplaced Central Venous Pressure Catheters.

Dr. George Wilson: We have seen two patients in the last few months with "missing" venous pressure catheters. X-ray revealed one catheter coiled in the right pulmonary artery of an 82 year old lady and the other in the superior vena cava and right heart of a 12 year old boy. In both cases the patient had multiple doctors, and each doctor thought another had removed the catheter, which actually had slipped off the needle and migrated centrally. I think that a progress note should be written when a catheter is removed. Of course these catheters should be well anchored to the skin to prevent migration.

Dr. Gerald Strauch: I would like to congratulate Dr. Schweizer on a real service to the Society. This paper points out very well some of the possible pitfalls in the management of central venous pressure catheters. At the Stamford Hospital we too have seen catheters all over the place including the right hepatic vein, when we inadvertently obtained some wedged hepatic venous pressures. We have also seen a rather substantial hemorrhage into the mediastinum from perforation of the left innominate vein.

Dr. John Fenn: I assume from Dr. Schweizer's presentation that he feels that the right atrium is a suitable place to leave a central venous catheter. One other hazard that we reported fairly recently was the placement of a central venous catheter with the tip in the right atrium and a subsequent severe arrhythmia which may have contributed to a fatality in a young girl. At autopsy there was a subendocardial hemorrhage in the region of the SA node, just in the place where a whipping catheter tip might have produced damage. Will Dr. Schweizer comment on what he feels is the ideal location for the central venous catheter?

Dr. Martin Dinep: We had a similar case about a week ago with an atrial fibrillation, and as soon as we pulled the catheter back the fibrillation stopped. Septicemia with or without septic thrombus or embolus due to infection around the catheter is another common complication.

Dr. Mark Hayes: We had an interesting experience not long ago with intravenous hyperalimentation. Septicemia due to nocardiosis occurred, and apparently this organism likes to grow in the sugar solution which comes out at the end of the centrally placed catheter. Dr. Schweizer, would you like to close?

Dr. Robert Schweizer: I would like to thank the discussants. I think the only question was what I think is the best place for a central venous pressure catheter. I personally think the catheter tip should lie in the superior vena cava just outside the right atrium. Thank you.

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The Zinc Story: An Introduction

Donald F. Bradley, Jr., M.D.

Of the 10 trace metals now known to be essential for human life, zinc appears to have the most direct effect on the healing process. In 1869, Raulin[1] first demonstrated that zinc was essential for the growth of Aspergillus niger. Zinc is one of 16 essential elements for the growth and fruiting of higher plants[2] and is receiving considerable attention because of reported zinc deficient soils in 32 of the 50 states.[3] In plant life, if one experimentally allows the plant to exhaust its supply of zinc, the earliest metabolic lesion to be detected is failure of RNA formation, followed closely by failure to form protein, total nitrogen, and DNA.[4, 5] As the zinc deficiency becomes more severe, the absolute amount of RNA falls. It appears that the RNA of zinc-deficient plants may be unstable. A possible explanation may be found in the discovery that zinc and other metals are normal constituents in the RNA of various plants, and it is postulated that zinc may be necessary to protect the RNA from nucleases.

Zinc in man has been shown to be an essential part of the following metalloenzymes:[6]

Carbonic Anhydrase
Alcohol Dehydrogenase
Carboxypeptidase
Tryptophan Desmolase
Malic Dehydrogenase
Glutamic Dehydrogenase
Lactic Dehydrogenase
Alkaline Phosphatase
Several Pyridine Nucleotide Dehydrogenases

There are other enzymes in which zinc appears to play an integral and necessary role, but probably in the form of a co-factor or catalyst. Of interest is the fact that substitution of zinc in one of the "simpler" metalloenzymes, e.g.—carboxypeptidase, by another group II B metal such as cadmium, inactivates the peptidase activity, the esterase activity remaining intact.[7] This potential for substitution and consequent inactivation opens fields of inquiry with direct application to present problems of water and air pollution, the recent deaths from cobalt-rich beer, and the trivalent chromium therapy for diabetes mellitus in the over-40 age group. However, these facets of trace metal metabolism are outside the purview of this introductory paper.

Strain et al[8] became interested in the systemic use of zinc after a laboratory accident in which a remarkable acceleration of healing occurred in a group of rats fed contaminated diets. Experimentation carried on between 1951 and 1954 using full-thickness wounds and burns of the dorsum of rats, revealed that the rats fed a methionine-zinc diet "healed more quickly than the controls".[9] To test the hypothesis that zinc is actually involved in wound healing,[10] radioactive zinc-65 chloride was administered intravenously to rats with abdominal wound incisions. As a control, similar studies were carried out by comparison with injected Sodium Iodide_{131}. Additional controls were carried out by comparing the radioactivity of the healing wounds with the adjacent skin and muscle. More zinc-65 accumulated in the wounds than in the surrounding tissues and rapidly showed a maximum in the wounds on the fifth to seventh days. On the 17th day, the wounds still had slightly greater radioactivity than the adjacent skin. The levels of NaI_{131} showed no difference after three days. After 100 days, there was still zinc-65 in most tissues, but none in the scar.

In a parallel study at the Brooke Army Hospital,[11] hair samples from 47 patients with thermal burns were analyzed for zinc. There was noted a rapid initial drop in zinc levels which only began to return to normal after 90 to 120 days. In a now classic study, Pories et al[12] operated upon 20 young airmen with chronically draining pilonidal sinuses. The wounds were allowed to heal by secondary intention, and at five day intervals, the wound volumes were measured using a JELTRATE (TM) cast of the wound cavity. Ten of the airmen were selected to be given, in addition to their regular diet, zinc sulfate 220 milligrams three times a day. The significant acceleration of wound healing is well demonstrated: the control group with a smaller mean wound volume of 32.2 ml. required 80 ± 13.7 days for complete healing, whereas the treated group with larger mean wound volumes 54.5 ml. required 45.8 ± 2.6 days for complete healing.

To consider some of the other facets of zinc metabolism: in 1961. Prasad et al[13] studied 11 Iranian male adults who had severe iron deficiency

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anemia, massive hepatosplenomegaly, dwarfism, marked hypogonadism, a history of geophagia (clay), and no evidence of chronic blood loss or parasitism. All were treated with a good hospital diet, pharmaceutical ferrous sulfate (1.0 gram per day) with rapid correction of the anemia, improvement of the hepatosplenomegaly, growth of pubic hair, and an increase in the size of genitalia. However, it was readily apparent to the investigators that the presenting signs and symptoms were not those of iron deficiency anemia. Prasad[14] had the further opportunity to study a similar group of 11 Egyptian males. He was able to divide the 11 men into three categories, six were treated with reagent zinc sulfate 90 mgms. per day; three were treated with reagent ferrous sulfate 1.0 gm. per day (pharmaceutical $FeSO_4$ having been found to contain varying amounts of zinc as a contaminant); and the remaining two returned to their village, having refused treatment, and thereby acting as controls. Of those treated with reagent zinc sulfate, all grew five to six inches in height within one year with a rapid increase in the size of their genitalia, appearance of pubic hair, decrease in hepatosplenomegaly. However the serum iron and hematocrit showed no change. The three patients treated with reagent ferrous sulfate, grew 2½ to three inches per year. One male, after a year's therapy with iron, was started on a course of zinc sulfate and grew six inches. In the ferrous sulfate treated group, there was a prompt rise in hematocrit and serum iron concentration, but no changes in genitalia or secondary sex characteristics.

Regarding zinc and its relation to the vascular system, experimentally it has been noted that the aortic wall has an extremely rapid turnover of zinc-65.[15] By the tenth day after injection, the zinc-65 concentration in the aorta is higher than in any other tissue. When the arterial wall is injured, the zinc-65 becomes even more active, tripling during the first week of healing. In a group of 39 patients with proven atherosclerotic occlusive disease who had inoperable ischemic symptoms, Plecha et al[16] treated them with zinc sulfate 220 mgms. three times a day for up to 36 months. Each patient was evaluated with arteriography, oscillometry, palpation of pulses, capillary and venous filling times, and exercise tolerance tests. Of the 39 original patients, 36 were followed sufficiently long for evaluation. Of these 36 patients, 30 (86%) improved symptomatically with increase of exercise tolerance, and 14 (39%) developed return of previously absent pulses. Arteriography was repeated in patients after one year, but showed no change in the major vessels. However, there was noted an increase in collaterals. The patients who benefited from zinc therapy had lower initial serum zinc levels than those patients not particularly benefited.

Further corroborative evidence of the relationship between zinc and arterial disease has been suggested in three other separate studies. Strain et al[17] studied 25 males who had proven atherosclerotic disease (either by arteriography or arteriography plus surgery) and found that the median hair zinc level was 62 ppm. as opposed to 125-150 ppm. in the normal. Volkov[18] studied 72 patients with atherosclerosis and noted significant decreases in the zinc content of the plasma, aorta, liver, myocardium, and pancreas. Wacker[19] reported mean plasma zinc values of 67 ± 13 micrograms % in patients with myocardial infarctions, as opposed to a mean normal plasma zinc level of 120 ± 19 micrograms %.

Finally, in a series of laboratory studies, Hurley[20] reported gross congenital malformations present in 90% of the young produced by normal adult female rats subjected to a zinc deficient diet throughout pregnancy. Of note is the fact that these same females also had about half as many young per litter as did the control animals who received 100 ppm. of zinc. The birth weights of the zinc-deprived offspring were half those of the young born to control animals. It appears that short periods of zinc deficiency during pregnancy were teratogenic; 22% of the young were malformed in females given a zinc-deficient diet from day-0 to day-10; 46% were noted to be malformed when the deficient diet was extended from day six through day-14.

In summary: although the necessity of protein, carbohydrate, lipids, and vitamins in wound healing has long been recognized, it is only recently that metals have been shown to play an important part in tissue repair. It appears that metals probably act in concert with a number of essential enzyme systems,. At the present time, zinc seems to be the most important of these. It is hoped that an increasing awareness and understanding of these relationships will stimulate the use of trace metal medication in the hope of alleviating some of the serious healing problems so often seen in surgical patients.

Discussion of Dr. Donald Bradley's paper: The Zinc Story: An Introduction.

Dr. Ira Goldenberg: I have the impression that we might be giving zinc to everybody. Are there toxic effects? Is pharmaceutical zinc sulfate available?

Dr. Donald Bradley: The sulfate salt of zinc has been used many years as an emetic. Its toxic dose is 15 gms. a day. The therapeutic dose is 220 mgs. of the sulfate three times a day. It should be given with meals. It is perfectly safe. It is a gastric irritant which behooves one to give it with a meal. Zinc chloride on the other hand is an instant escharotic and is extremely corrosive. It will ulcerate, if not through the stomach, rapidly through the jejunum or duodenum. It shouldn't be given at all. However, zinc chloride can be given intravenously if diluted. It is available depending upon the pharmacy one uses.

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Present Status of Augmentation Mammaplasty

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As the 20th century female becomes more conscious of esthetic values, correction of hypoplastic and large breasts is more in demand. Furthermore, as the profession and the public become more aware of preventive medicine, subcutaneous mastectomies with benign mastopathies are frequently performed with simultaneous reconstruction of breasts.

In patients with moderate and larger size breasts, enough local tissues can be saved for breast reconstruction after subcutaneous mastectomy. A paper describing such a satisfactory operation was presented to this Society by the author 13 years ago.[2, 3]

The content of this paper deals with the augmentation of small breasts, its complications and end results. To increase the size of breasts autogenous material such a gluteal fat etc., was first used with rather unsatisfactory results due to hardening, shrinkage, and fat necrosis. About 18 years ago, Pangman recommended the use of alloplastic materials which has lead to the development of many improved prostheses giving the desired form and consistency with apparently permanent result.

How safe are these implants in the human body? It is estimated that during the last two decades several hundred thousand silicone implants, such as artificial heart valves, hydrocephalus shunts, silicone rubber for detached retinas besides those for noses, chins, and other soft tissue areas, were inserted into the human body without any known oncogenic effect.

To gain more knowledge of the current status of augmentation mammaplasty a world wide survey was conducted by the author. 10,941 cases were reported by 265 qualified plastic surgeons with up to 18 years of follow-up. With 'open pore' sponge like prostheses, (Etheron, Ivalon, Polurethane, etc.,) the results were not too satisfactory, since the prostheses hardened and shrank. Loss of symmetry, due to fibrous tissue ingrowth, often necessitated replacement by the 'balloon type' implants, (Cronin Type, Simaplast and Ashley Type). Such implants containing fluid cannot be compressed by scarring. The form of the breast remains constant and there is minimal hardening, since a fibrous membrane is formed in a short time around the implant without any tissue ingrowth.

The survey disclosed that 80% of the patients were between 16 to 30 years of age, 15 between 30-40 and 5 over 40. The overall rate of infection was 2½% after operation. Two thirds of these infections occurred immediately after operation and one third were late in appearance. When implants were immediately inserted after subcutaneous mastectomies the rate of infection was 5%. Late complications[1] such as skin-perforation rose to 16% as compared to 2% after augmentation mammaplasty. This high complication rate may have resulted from the use of overly large implants, or their placement under thin, scarred skin. Fluid accumulation and leakage was frequently observed which subsided with 4 to 5 weeks of conservative treatment. In cases where aspiration was required with positive bacterial culture, some of the inserts had to be removed.

A few patients have complained of palpation of the edge of the prostheses. Pregnancy and nursing have been successfully accomplished by women after augmentation mammaplasty. The more serious complications of cyst formation and skin necrosis have only been seen with silicone injection,[4] the use of which is now illegal.

The most interesting complication to consider is neoplasia. Do these protheses effect the incidence of tumor formation in an organ already prone to develop new growths?

The incidence of benign tumors after augmentation mammaplasty is reported as 0.2%. Only seven cases of carcinoma of the breast are reported in the surveyed 10,941 patients, many of whom were over 30 years of age.[5, 6] Will the incidence of carcinoma eventually prove to be lower in women after augmentation mammaplasty than in normal controls—perhaps due to the small volume of breast tissue, or will prolonged follow-up data reveal a late incidence of breast cancer perhaps 20-40 years after augmentation mammaplasty?

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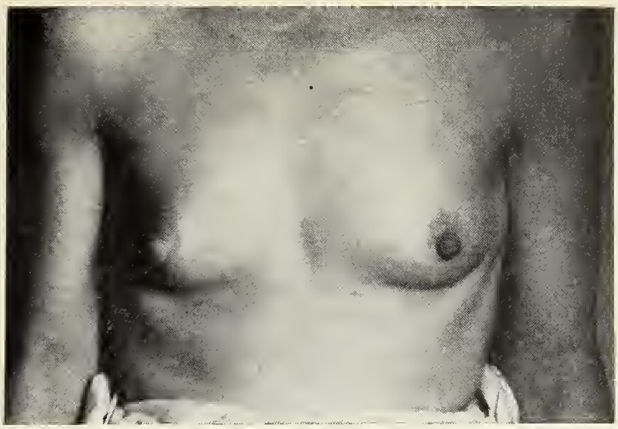

Figure 1

Hypoplastic Breasts of a 22 year old woman.

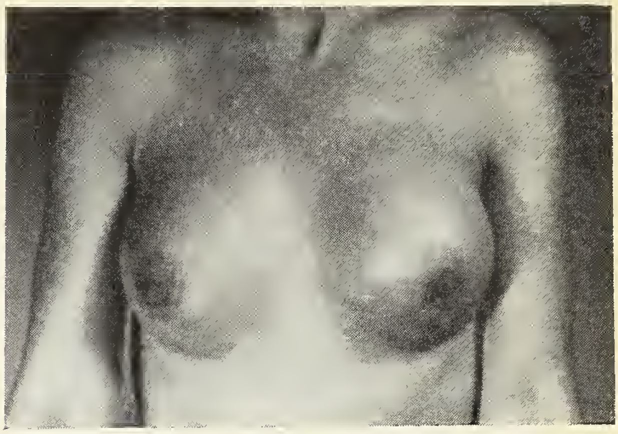

Figure 2

After Augmentation Mammaplasty:

For the present it can only be said that the human patient has not shown the oncogenic reaction of certain rodents to foreign body implants. However, before augmentation mammaplasty it is wise to discuss with the patient the normal occurrence of breast carcinoma and the scientific evidence accumulated to date about the relationship of mammary prosthesis to carcinogenesis.

Summary

A world wide survey of the results of augmentation mammaplasty has been made. Complications are infrequent after operation performed by experienced surgeons. The question of carcinogenesis remains unanswered, but the data collected to date have not shown any increase of breast cancer in patients followed up to 18 years.

*Discussion of Dr. Cholnoky's paper: The Results of a World Wide Survey on Augmentation Mammaplasty.**

Dr. John Standard: Would you recommend immediate augmentation mammaplasty after subcutaneous mastectomy in a young woman with sclerosing adenosis as an answer to the problem of multiple biopsies and a continuing fear of cancer? We have done this in women with lobular carcinoma in situ. These immediate protheses have worked very well. Is there any series of similar cases?

Dr. Paul Gerity: I wonder if Dr. Cholnoky would comment on the office injection of silicone.

Dr. Tibor de Cholnoky: I agree that removal of all of the breast tissue in patients with sclerosing adenosis or cystic mastitis is a good solution to the patient's problem. With breast carcinoma, breast reconstruction may be done after the radical operation—but preferably at a later date when the cancer is controlled. There are no reports of immediate reconstruction following cancer operations. In the moderate or large sized breast, after the removal of the diseased gland, enough local tissue can usually be saved for immediate reconstruction of the breast.[2] This report is given only to alert you to the fact that silicone prostheses can be implanted with minimal morbidity and without any known risk of cancer. Breast reconstruction with autogenous tissue, whenever it is feasible, is still preferred. To my knowledge, the Food and Drug Administration has not yet released silicone injection fluid for general use because of the serious complications which have been repeatedly observed.

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Transduodenal Sphincterotomy and Choledocholithiasis

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Surgeons performing biliary tract surgery recognize that in spite of meticulous common duct exploration, a significant number of retained or reformed stones are ultimately demonstrated postoperatively by X-ray and at re-operation. The quest for the perfect common duct exploration has led numerous investigators to devise ingenious methods to achieve a uniform procedure for detection and removal of all stones at operation. No single method to date has guaranteed the precise detection and removal of all common duct stones.

The first transduodenal sphincterotomy in the Windham Community Memorial Hospital was performed in 1949. During the subsequent 18 years, 123 transduodenal sphincterotomies were performed for pancreatico-biliary tract disease. During the same time interval, 806 biliary tract procedures were performed. Of the 806, 73.3% of the procedures were limited to a cholecystectomy. Ninety-two or 11.4% resulted in a simple common duct exploration; 123 or 15.3% included the transduodenal sphincterotomy and common duct exploration. Of the 123 sphincterotomies, 36 procedures were performed for recurrent pancreatitis. The follow-up on these patients is virtually complete at 99%. The average follow-up is 8.3 years ranging from 6 months to 18 years. This analysis is a personal series of cases including those of the authors and Dr. Edward J. Ottenheimer who was a former member of this society.

This discussion is limited to the analysis of the overall results of the use of the addition of transduodenal sphincterotomy to the maneuver of common duct exploration in the treatment of choledocholithiasis. Of pertinent interest in the study are the following questions: (1) What are the comparative results in terms of morbidity and mortality between the simple common duct exploration and the common duct exploration plus transduodenal sphincterotomy? (2) Is the incidence of residual or recurrent calculi different in the two procedures? (3) Finally, what are the indications for the use of transduodenal sphincterotomy in the treatment of choledocholithiasis?

Results

The overall complication rate, i.e. major and minor, for the entire series was 17.8%. The reports of others list morbidity rates for simple common duct exploration varying from 10 to 25%. Wound complications occurred in 8.9% of our cases. Four per cent of the patients experienced cardiopulmonary complications. The majority of complications occurred in elderly individuals with acute illnesses associated with jaundice.

The overall postoperative death rate was 3.3% which parallels that of common duct exploration. Seventy-one per cent of the patients were still alive for analysis. Thirty-one deaths unrelated to operation occurred in the follow-up period. Of the four hospital deaths, three of the four hospital deaths occurred in patients presenting with acute cholecystitis and jaundice who were over seventy-five years of age. Only one hospital death was directly attributed to the operation. Postoperatively, this patient developed a duodenal fistual with a retroperitoneal abscess.

In reviewing the literature, the percentage of recurrent calculi following common duct exploration varies from 1 to 28%, with the average being approximately 5 to 10%. In the present series of 123 patients, stones were found in the common duct of 54 patients. In follow-up, three of these 54 patients were found to have retained or reformed stones in the common duct. This represents a recurrence rate of 5.6% or 2.4% when calculated against the entire series.

No patient with an initial duct exploration in which no stones were found ever returned with choledocholithiasis. Of the three individuals in whom recurrent stones were discovered, one individual was thought to have a satisfactory operation with a normal discharge cholangiogram. In spite of this, stones were recovered at another hospital at re-operation. The course of the two other patients might have been changed had more study been

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given to their discharge cholangiograms. In at least eight of the 51 remaining patients initial common duct exploration was negative and it is felt that stones would have been overlooked and a secondary procedure would have been required had not transduodenal sphincterotomy been performed. This would raise the recurrence rate from 5.6% to approximately 20%. This factor is of great importance when one considers that mortality rates increase from five to 15% with recurrent operative procedures on the common duct.

Discussion

The search for better ways to detect and remove common duct stones is a continuous process. Accepting the imperfections of the common duct exploration and operative cholangiography, the following criteria have been used in extending the common duct exploration to include a transduodenal sphincterotomy: (1) Many small stones and sludge discovered in the common duct (2) A tight sphincter not allowing passage of a #3 Bakes dilator (3) History of recurrent pancreatitis (4) Dilated common duct with a history of jaundice (5) An operative cholangiogram which is not explained on the simple basis of choledochotomy (6) When there is a suspicion of ampullary pathology.

Transduodenal sphincterotomy is not recommended as a routine procedure in the treatment of choledocholithiasis. The procedure is limited to a simple common duct exploration when large stones are present in the duct along with clear bile when there is widely patent ampulla, and when a post-choledochotomy cholangiogram is thought to be normal. Transduodenal sphincterotomy should be utilized if all other methods fail to produce a satisfactory exploration of the common duct. With transduodenal sphincterotomy a more thorough examination of the common duct will be performed. In our experience sphincterotomy is not attended by an increase in morbidity and mortality rates. Stones which might have been overlooked will be retrieved. Furthermore, stones which might have been overlooked might very well pass during the postoperative period. At the present time, the permanency of the physiological effect of transection of the sphincter of Oddi depends upon the adequacy of the sphincteroplasty performed at the time of operation.

Discussion of Dr. Whalen's paper: Transduodenal Sphincterotomy.

Dr. William Livingston: Recurrent attacks of upper abdominal pain and fever followed sphincterotomy in one of my patients. A barium contrast study (slide) revealed reflux into the common bile duct. Would Dr. Whalen comment upon the incidence of ascending cholangitis after sphincterotomy or sphincterotomy?

Dr. Robert Houlihan: Dr. Whalen, do you routinely use a long armed T-tube after sphincterotomy?

Dr. Mark Hayes: You know a lot of this is terminology. Sphincterotomy may mean a little "snip" to some and an end-to-side choledochoduodenostomy to others.

Dr. William Whalen: S. A. Jones evaluates the adequacy of sphincterotomy by testing yield pressures postoperatively with and without morphine injection and with cineradiography. He also determines whether there is retrograde passage of barium into the common duct after a barium meal. If there is he feels, that a satisfactory sphincteroplasty has been performed. We have had no instances of postoperative cholangitis in our cases. As I recall, Dr. Jones didn't report this either. What we are trying to do with sphincterotomy is to accomplish the complete removal of common duct stones. All of the other methods having their shortcomings, I don't know whether it is possible to entirely eliminate the incidence of retained or recurrent common duct stones, but I do believe that it is possible to decrease the recurrence rate to a respectable level by judicious use of sphincterotomy.

It is not true that the spincterotomy effect lasts only for a week or two. Eiseman and Lempke have demonstrated that sphincter incompetence persists approximately six to eight weeks. Small stones will probably pass during this time. Then the sphincter will close down again unless the musculature of the sphincter and also the duodenal wall has been transected as recommended by Jones.

We don't routinely use the long armed T-tube after sphincterotomy. There were 35 long armed T-tubes used during the course of this analysis over the last 20 years, and in no case was there pancreatitis produced from this. At the present time we use a short armed T-tube.

THE PRESIDENT'S PAGE

As I have noted in previous President's Pages, the problem of improving the delivery of health care services is a most pressing one at this particular point in time. Many agencies, both public and private, are concerning themselves with attempting to deal with it effectively. Quite recently, Regional Medical Programs have declared their interest and involvement in the restructuring of the American health care system. To fully appreciate the implications of this declaration, it is important to review the origin and development of RMP's in general and of the Connecticut agency (CRMP) in particular.

Regional Medical Programs were created by an act of Congress which was signed into law by President Johnson in 1966. The legislation stemmed from a study made by a Presidential Commission, chaired by Dr. Michael DeBakey, which found (among other things) that the benefits of modern scientific research in the fields of heart disease, cancer and stroke were not being made available to all segments of the population. The Commission proposed that attempts be made to remedy this situation through a combination of education, demonstration and research in the subject fields. The creation of RMP's constituted the Congressional response to this proposal, adding the category of "related diseases" as a means of providing some latitude to the potential scope of Program activities. In its wisdom, however, the Congress stipulated that such education, demonstration and research projects were to be carried on *without interfering* with established methods of delivery of, or payment for, medical care.

In implementing the law for Connecticut, Governor Dempsey designated the state's two medical schools as the grantees to study and plan for a regional medical program, with the Yale School as the principal grantee since the UConn School was then still in its infancy. A CRMP Advisory Board and Executive Committee were appointed, and, shortly thereafter, a Director was employed to administer the affairs of the Program. Subsequently, an elaborate structure of Task Forces, Advisory Conferences and the like came into being and planning activities were begun with considerable enthusiasm and fanfare.

During the early months of CRMP's development the Society's Council received, and complied with, many requests for the nomination of member physicians to serve with the various Task Forces and Advisory Conferences. The "feedback" to the Council from these representatives, however, was characteristically rather spasmodic and fragmentary and a great deal was left to the imagination as to what, exactly, was being studied and what sort of course the studies would set for RMP in Connecticut.

The Council's first real opportunity to learn about the trend and "flavor" of early CRMP planning came when it made an in-depth study of the Program's 1968 Grant Request for Federal operating funds. Over and above criticizing several specifics of the Grant Request (too little representation of practicing physicians; too much "planning from the top"; inadequate preparation for proposed elaborate projects; etc.), the Council voiced strenuous objection to one of the major premises of CRMP's "grand design"; i.e., that the existing system of medical care in Connecticut was looked upon "in many quarters" as being quite unsatisfactory and that, hence, CRMP saw as one of its major "missions" the providing of a method to *change* the system so as to eliminate this general dissatisfaction.

Responding to this latter objection of the Council, the CRMP Board and staff declined to identify even one of the "many quarters" referred to in the Grant Request. It was suggested that the Council not give too literal an interpretation to the wording of the Request—that it was "too early to say" just what some of these words and phrases might come to mean in the years to come and that even some members of the agency's Advisory Board had far from a full understanding of what CRMP was all about or would eventually prove to be all about.

Having been given these assurances, the Council adopted a wait-and-see policy on this important matter—hoping that well planned and executed programs of education, demonstration and research would result in improved patient care in Connecticut *without* interfering with established patterns of delivery and financing. During the next year or so it appeared that, with some minor exceptions, progress was being made by CRMP toward accomplishing the former objective while paying heed to the latter statutory prohibition.

Recently, however, there have been developments which indicate rather clearly that the Council's original apprehension concerning CRMP's ultimate goals were all too well founded. The agency has, in fact, continued to go the way it planned and set forth in its 1968 grant request for operating funds. It now publicly proclaims that "CRMP is concerned with the delivery of the best possible health care to all 3,000,000 citizens of Connecticut in the most efficient way, with special concern for victims of heart disease, cancer and stroke but not limited to these diseases. This means that CRMP focuses on *quality* of care, on *service to all* including the disadvantaged in the inner city and on *economy* of delivery of health services." (CRMP Newsletter, ibid). This grand strategy is further enunciated in its Request for a Supplemental Grant July 30, 1970 to be acted upon by the National Advisory Council at its November 1970 meeting.

Most bureaucrats strive to increase their domain. We see this repeatedly in governmental and non-profit agencies. Not content to devoting themselves to improving the care of the patient with Heart Disease, Cancer and Stroke, the Regional Medical Programs are now to concern themselves with producing "the changes which we clearly need for an effective health care system." This from the Acting Director of the Regional Medical Programs Service, Dr. Harold Margulies, in a talk on "Trends in Health Care" delivered at the annual meeting of the Iowa Regional Medical Program on June 26, 1970 (as reported in *CRMP Newsletter,* Vol. I, No. 18; Sept. 28, 1970). He is further quoted as stating that the Regional Medical Programs are a sort of political-social instrument and he charges the Regional Medical Programs with solving many of the problems facing medical care delivery today,–quality control, cost control, utilization, health manpower, use of allied health personnel, etc. This is alarming but also sad. To think how many patients with Heart Disease, Cancer and Stroke might have been helped since the legislation was enacted in 1966 if the bureaucrats in Washington and elsewhere had devoted themselves to implementing the intent of the legislation rather than enlarging their domains.

The Problem posed by CRMP's involvement in the health care delivery system is serious. CRMP has not shown itself to be responsive to the needs of the people or the physicians of Connecticut. It is dedicated to a "grand strategy" formulated without any knowledge of Connecticut and its problems. Furthermore the philosophy of its "core staff," as described in the Grant Request, and the power generated by its access to huge sums of money may be harmful.

MORRIS A. GRANOFF, M.D.

FROM THE EXECUTIVE DIRECTOR'S OFFICE

160 St. Ronan Street, New Haven, Conn. 06511
Telephone 865-0587

Raymond T. Sullivan, Jr.
Assistant Executive Director
Public Affairs

William R. Richards, M.D.
Executive Director
Josephine P. Lindquist
Associate Executive Director

Leonard R. Tomat
Assistant Executive Director
Scientific Activities

SUMMARY OF ACTIONS COUNCIL MEETING

Wednesday, September 16, 1970

I. Attendance

Present were: Drs. Granoff, Weber, Jr., Grendon, Burnham, Edson, Abbot, Dean, Gardner, Fabro, Rem, Harwood, Pelz, Palomba, Roch, Van Syckle, Friedberg, Johnson, Ragland, Jr., Freedman, Root, Jr., vonGlahn, Purnell and Klare.

Also present were: Mrs. Lindquist, Mr. Tomat, Mr. Sullivan, Mr. Donelan (AMA), Dr. Redlich (Yale School of Medicine), Mr. Olson (FCMA) and Dr. Richards.

Absent were: Drs. Brandon, Martin, Cramer, McDonald, Wilson, Jr., Nemoitin and Gorin.

Presiding: In the absence of the Chairman, Dr. Martin, and the Vice-Chairman, Dr. Brandon, the meeting was chaired by Dr. Granoff, President.

Acknowledgement: Prior to commencing the regular business meeting, it was VOTED to convey the thanks of the Council to the governing Board of the Woman's Auxiliary to CSMS for the delightful luncheon which the Board had invited the members of the Council and the staff to share as guests.

II. Routine Business

Approval of Minutes

As printed and distributed, it was VOTED to approve the minutes of the meeting of August 13, 1970.

Life Memberships

It was VOTED to approve applications for Life Membership received from the following eligible Active Members:

Frederick M. Bannon, 300 Main Street, Stamford (FCMA)—1/1/71

John Brosnan, 293 Montauk Avenue, New London (NLCMA)—1/1/71

Grace V. Gorham, 64 Wall Street, Norwalk (FCMA)—1/1/71

Perry T. Hough, 232 Haynes Road, Avon (HCMA)—1/1/71

Jacob Nodelman, 26 Elm Street, New Haven (NHCMA)—1/1/71

Edward C. Rawls, 300 Main Street, Stamford (FCMA)—1/1/71

Edward Resnik, 272 Main Street, New Britain (HCMA)—1/1/71

Vincent T. Shea, 20 East Main Street, Waterbury (NHCMA)—1/1/71

Resignations, Appointments, Etc.

(a) *Committee on Public Relations:* It was VOTED to accept the resignation of John A. Woodworth, Moosup, as a County-designated member of the Committee. It was further VOTED to appoint Robert L. Painter, Putnam, to membership on the Committee as Dr. Woodworth's replacement for the balance of 1970-71.

(b) *Committee on National Legislation:* It was VOTED to appoint to membership on the Committee for the balance of 1970-71: Harry J. Tamoney, Jr., Hartford, and Eugene F. Lawlor, New Britain.

(c) *CHA Committee on Hospital Systems Engineering:* Responding to a request from the Connecticut Hospital Association, it was VOTED to nominate the following members for service with this CHA Committee: Kurt Pelz, Wallingford; Edward A. Rem, New Canaan.

Date of Next Meeting

The next meeting of the Council is scheduled for Thursday, October 29, 1970.

III. Old, New and Special Business

Nomination—Member of Connecticut Medical Examining Board

The President, Dr. Granoff, advised the Council that John D. Booth, Danbury, had resigned his appointment as a member of the Connecticut Medical Examining Board to Governor Dempsey (effective September 1, 1970), and that, by statute, the president of CSMS is required to nominate a replacement to the Governor for appointment. Dr. Booth's current five-year term is for 1/1/70-12/31/74. Dr. Granoff informed the Council that, after careful consideration of a number of possible qualified nominees, he had selected Franklin Robinson, New Haven, a neurosurgeon, to recommend to the Governor for appointment. After due discussion, and although not required to do so, the Council VOTED to confirm the president's choice of nominee, Dr. Robinson.

Format for 1970 Semi-Annual House of Delegates Meeting

As developed and recommended by the Ad Hoc Committee on Annual Meeting Arrangements, the Council VOTED to approve a detailed format for the 1970 Semi-Annual Meeting of the House of Delegates. In brief, the format calls for a full-day meeting (in contrast to previously traditional half-day sessions), the holding of reference committee hearings by the House sitting in "reference committee as if of the whole", and the reference committee reports to be projected on a screen while under consideration (instead of being reproduced by stencil and distributed in printed form).

Report—Subcommittee to Study and Revise the Bylaws

The Council acted on a series of reports filed by the Subcommittee as follows:

(a) *Members Under Suspension:* It was VOTED to approve the Subcommittee's recommendation that the present Bylaw provisions covering "suspension" of members from CSMS membership *not* be amended, and that the Hartford Association's Board of Directors be reminded that HCMA is free to submit a subject amendment of its choosing to the House of Delegates for consideration and action.

(b) *Membership for Osteopaths:* It was VOTED to approve the recommendation of the Subcommittee that membership applied for by osteopathic physicians licensed to practice medicine and surgery in Connecticut be considered on an individual basis by the component County Medical Associations, recognizing that the AMA is seeking increased liaison between M.D.'s and qualified D.O.'s and to encourage acceptance of osteopaths into the AMA organization. It was further VOTED to approve the Subcommittee's opinion that, since CSMS membership is contingent upon County Association membership and since no provision in the CSMS Bylaws precludes the acceptance of osteopaths as members, no subject amendment of the CSMS Bylaws is necessary to make such membership possible.

(c) *Major Revision of Bylaws:* It was VOTED to grant the Subcommittee's request that it be authorized to undertake a major revision of the CSMS Bylaws which, among other things, would remove most of the detailed provisions concerning committees (formation, election, function, etc.) from the Bylaws and thereby reduce the number and frequency of the amendments made in recent years—the majority of which have had to do with committees. It is understood that, in granting this authorization, the final product of the major revision would be subject to consideration and action by the Council and House of Delegates in accordance with the provisions covering all amendments to the Bylaws.

(d) *Resolutions:* It was VOTED to receive as information the statement of the Subcommittee that any member of the Society (Active, Life, Associate, Honorary or Student) may introduce resolutions at meetings of the House of Delegates in accordance with the Bylaws provisions covering the introduction of resolutions to the House.

(e) *Student Members:* It was VOTED to receive as information a report that the Subcommittee has under study the possibility of granting CSMS Student Members representation in the House of Delegates, perhaps on a per capita basis and with voting rights, and will file a more definitive report on this subject at a later date.

Report—Liaison Committee with the Welfare Department

A series of reports submitted by the Liaison Committee were acted upon as follows:

(a) *Minutes:* It was VOTED to receive as information the minutes of the Liaison Committee's meeting of 8/26/70.

(b) *Chairman's Report:* It was VOTED to receive as information the report of the Committee chairman, Charles Polivy, that progress is being made toward eliminating much of the "red tape" that has been associated with the requirement of "prior authorization" before certain types of services may be rendered to Medicaid beneficiaries.

(c) *Third Party Payments to Salaried Physicians:* It was VOTED to approve a recommendation of the Liaison Committee, and assign same to the Committee on Third Party Payments for study and report, that the Society "establish a policy on the question of third party payments being made to salaried physicians rendering services in teaching settings".

The CRMP-CUPISS Program

It was VOTED to receive as information, and with thanks, a letter from John D. Thompson, Ph.D., Professor of Hospital Administration at the

Yale Department of Epidemiology and Public Health and Principal Investigator for CUPISS, which purported to inform the Council of the provisions made in the CUPISS Program to protect the rights of patients (by legal standards), in the matter of confidentiality and "informed consent". with respect to feeding their medical and health record information into the CUPPISS computer systems. It was further VOTED to invite Dr. Thompson and Marvin Garrell, Fairfield, a CSMS representative on the CUPISS Technical Advisory Committee, to join the Council at the next convenient meeting to participate in an in-depth exploration of these matters (particularly from the legal standpoint) and to respond to such questions as members of the Council may have concerning same.

Progress Report—Committee on Professional Liability

The Committee submitted a report on the progress which had been made at its first two meetings. It was VOTED to receive as information a copy of the minutes of the initial meeting, held on August 19, 1970. It was further VOTED to act on several recommendations offered by the Committee as follows:

(a) To approve the Committee's action of submitting to the Committee on State Legislation, for appropriate study and legislative action, the problem of the vulnerability of malpractice records (such as the Committee might keep) to subpoena, particularly by a plaintiff's attorney.

(b) To approve the Committee's recommendation that the CSMS Bylaws *not* be amended, at this time, to provide for mandatory reporting of malpractice claims and suits as a condition of membership in good standing, and that this recommendation be transmitted to the next meeting of the House of Delegates in lieu of an amendment to provide for such reporting, as requested by the House on May 12, 1970.

(c) To approve the Committee's recommendation that the reporting of malpractice situations, past, current and future, be made a contingency of enrollment in a CSMS group malpractice insurance plan when such is made available to the membership, and that this recommendation be used *as a guide* by the Committee in developing such a plan with any and all prospective insurance carriers.

(d) To approve a recommendation of the Committee, as amended by the Council, that the secretaries of the component County Medical Associations be *requested* to file with the chairman of the Committee on Professional Liability bi-annual statistical (numerical) reports on malpractice actions against members brought to the attention of their respective Associations; also that, at this time, no subject amendment to the Bylaws is indicated.

Report—Manning the Capitol with Physicians

It was VOTED to accept, with thanks and commendation, a report filed by Kenneth F. Brandon, Hartford, on his investigation of the need and/or desirability of the Society seeking to arrange for physician volunteers to provide medical coverage for legislators while the General Assembly is in session. It was further VOTED to approve Dr. Brandon's recommendation that need for such coverage appeared *not* to exist and that the Society *not* seek to arrange for same at this time.

Reports—Michael A. Dean, Bridgeport

Two reports submitted by Dr. Dean were acted upon as follows:

(a) *Osteopathy:* It was VOTED to accept with thanks a report on the possible acceptance of qualified Doctors of Osteopathy into membership in Connecticut units of organized medicine (CSMS and the component County Medical Associations).

(b) *Length of Hospital Stay:* It was VOTED to accept a report on this subject, prepared by Dr. Dean on the basis of experience at St. Vincent's Hospital, Bridgeport, and to furnish copies of the report to members of the Committee on Hospitals for information and study.

Request for CSMS Policy Statement

In a letter to the Council, Arthur Ebbert, Jr., New Haven, reviewed briefly the past and present controversy (often in the public domain) as to the rights of imprisoned persons to receive medical care from a physician of their own choosing (rather than one furnished by the prison authorities), particularly if they are in prison as non-convicted persons in pre-trial detention; i.e., assumed to be innocent unless and until proven guilty. After lengthy discussion, which made it clear that members of the Council recognized this question as being multifaceted and complex, it was VOTED to refer the question to the Judicial Committee for in-depth study and comprehensive report to the Council.

N.B.: *The foregoing is a summary of the proceedings and actions of the Council on September 16, 1970. Detailed minutes of the meeting are on file at 160 St. Ronan Street, New Haven, for perusal by any interested member of the Society.*

Placement Wanted

DERMATOLOGIST—30 years of age, Eligible with National Boards wishes solo type practice in a medium or small size community in Connecticut. (Perferably not too far from a large city). Presently in practice.

GENERAL PRACTICE—32 years of age, with National Boards, wishes group type practice in Connecticut. Available in November when military obligation completed. Contact: Lee M. Dippery, Major, MC, M.D., H.Q. 6/10 Field Artillery, New York APO 09139.

GENERAL PRACTICE—30 years of age, wishes solo, associate or institutional type practice in a small community in Connecticut, Military obligation completed.

INTERNIST—38 years of age, Eligible wishes group or industrial type practice in Connecticut.

Will consider any position. Connecticut license. Presently available. Contact: Declan Foley, M.D., 76 North Pearl Street, Meriden, Connecticut 06450.

INTERNIST—46 years of age, Certified with National Boards, wishes group, institutional or industrial type practice in Connecticut. Presently in practice. Connecticut license. Available immediately.

INTERNIST—34 years of age, Eligible, wishes associate or institutional type praceice in Connecticut. Presently in practice.

INTERNIST—34 years of age, Eligible wishes solo, associate or group type practice in Connecticut. Connecticut license.

INTERNIST—32 years of age, qualified (and Eligible), with National Boards and Connecticut License, two years experience in cardiology wishes to join group or associate type practice in southern Connecticut. Military obligation completed.

INTERNIST—36 years of age, Eligible, wishes group or institutional type practice in a medium or small size community in Connecticut. Presently in practice. Prefer hospital-based group or full-time.

INTERNIST/CARDIOLOGY—30 years of age, Eligible with National Boards wishes associate type practice in a medium size community in Connecticut. Would like to associate with 1-3 other Internists. Military obligation completed.

INTERNIST—45 years of age, Certified, wishes group, institutional or industrial type practice in Connecticut. Available immediately. Contact: John G. Swadey, M.D., 132 Phillips Road, Pembroke, Mass. 02359.

INTERNIST—33 years of age, Eligible with National Boards, wishes group, associate or institutional type practice in a large or medium size community in Connecticut.

NEUROSURGERY—35 years of age, Certified, wishes group, institutional or academic type practice in a large or medium size community in Connecticut.

NEUROSURGERY—32 years of age, Eligible with National Boards, wishes solo or associate type practice in Connecticut.

OBSTETRICS & GYNECOLOGY—33 years of age, Eligible with National Boards, wishes group type practice in a medium size community in Connecticut. Presently in practice. Military obligation completed. Contact: Stephen B. Berkowitz, M.D., 415 Grand Street, Apt. 1801, New York, New York 10002.

OBSTETRICS & GYNECOLOGY—34 years of age, Eligible, wishes group or associate type practice in a medium size community in Connecticut. Military obligation completed in January 1971.

OPHTHALMOLOGIST—31 years of age, Eligible wishes to practice in Connecticut. Connecticut License. Extensive subspecialty training.

PATHOLOGIST—39 years of age, Certified with National Boards, wishes associate type practice in a medium size community in Connecticut. Connecticut license. Desires position as chief Pathologist or laboratory director. Contact: Sanford H. Edberg, M.D., Lee Hospital, 320 Main Street, Johnstown, Pennsylvania 15901.

PATHOLOGIST—35 years of age, with National Boards, wishes group, associate or institutional type practice in Connecticut.

PATHOLOGIST/ANATOMIC—48 years of age, Certified, wishes institutional type practice in Connecticut. Presently in practice. Would perfer an academic center, since interested in routine work, teaching and research. Available early 1971.

PEDIATRICIAN—47 years of age, Certified, wishes group or associate type practice in a large or medium size community in Connecticut. Presently in practice.

PEDIATRICIAN—33 years of age, Certified, wishes solo, group, associate or institutional type practice in a large or medium size community. Academically oriented practice prefer medical school affiliation. Available immediately.

PEDIATRICIAN—40 years of age, Eligible, wishes solo, group or associate type practice in a medium or small size community in Connecticut. Available immediately. Contact: Vasant G. Yadav, M.D., 201 W. Cuthbert Blvd., Oaklyn, New Jersey 08107.

SURGEON—33 years of age, wishes group or associate type practice in Connecticut. Certified with National Boards. Available immediately.

SURGERY—28 years of age, Eligible, wishes solo, group or associate type practice in Connecticut.

Placement Opportunities

ANESTHESIOLOGIST—position available for associate to board-certified anesthesiologist in an attractive progressive general hospital. Excellent staff. Generous remuneration. Minimum amount of call with maximum vacation time. Write or call: Dr. Marvin Albert, World War II Veterans' Memorial Hospital, Paddock Avenue, Meriden, Connecticut 06450. Telephone 203-237-5531.

DISTRICT HEALTH DIRECTOR for Westport/Weston, Connecticut. Requires M.D., degree in Public Health or equivalent experience, and eligibility for Connecticut license. Salary range $22,000 to $26,000 depending on qualifications. Population served, 35,000. Excellent schools cultural and recreational opportunities. Position available October, 1970. Send resume to Clifford W. Mills, M.D., Chairman, Aspetuck Valley Health District Board, 180 Bayberry Lane, Westport, Connecticut 06880.

OPPORTUNITY FOR INTERNIST OR GENERAL PRACTITIONER for association with General Practitioner. A good family practice in urban community in Connecticut. No Ob or major surgery. Part-time University position if desired.

Part-time University position if desired.

OBSTETRICS & GYNECOLOGY—Board eligible or rated, to immediately take over 20 year successful solo practice. Costal Fairfield County. Token investment. Will introduce if available. Connecticut license required. Must be available soon. Incumbent leaving area permanently. Lease available.

OFFICE/HOME combination for sale. Connecticut shoreline. Seven room office fully equipped including X-ray, fluoroscope, EKG etc. Dark room and laboratory. Excellent opportunity for immediate income from active, lucrative practice. Close proximity to Yale New Haven Medical Center and Middlesex Memorial Hospital, Middletown, Connecticut. Physician recently deceased. For details write to: P.O. Box 222, Clinton, Connecticut 06413.

PATHOLOGIST—Board certified AP-CP with 3-5 years experience, to associate with director of modern laboratory in accredited voluntary hospital nearing completion of expansion to 400 beds. Active teaching program for interns and residents; medical school affiliation. Write: Dr. I. Rothstein, Mount Sinai Hospital, Hartford, Connecticut 06112.

PEDIATRICIANS—Two board certified Pediatricians seek dynamic young associate to join rapidly expanding practice and medical community for the general practice of Pediatrics. Excellent salary to partnership. Equal time off. No investment necessary. For further information contact: Thomas J. McGrath, M.D., 108 New London Turnpike, Norwich, Connecticut 06360. (203) 889-3835.

PEDIATRICIANS—opportunity in area of 75,000 for hospital-based private practice or community-based private practice. Modern 250 bed, Yale affiliated, general hospital in Southern Connecticut suburban community. Excellent diagnostic services available. Attractive living conditions. Reply to: Administrator, Griffin Hospital, Derby, Connecticut 06418.

PHYSICIANS—Five room office fully equipped with X-ray and laboratory. Located in beautiful southern Connecticut shoreline area. Six blocks from Community Hospital, which is expanding. The hospital is the only one within 45 mile radius. Community over 40,000 people which consists of several small towns with population 3,000 to 14,000 each.

PSYCHIATRIST—Full and part time positions available at progressive Mental Health Center. Located in central Connecticut, near large eastern universities and Metropolitan areas of Hartford, New Haven and New York City. Minimum requirements: 3 years approved psychiatrist, residency training and eligible for Connecticut license. Salary range $23,227 to $28,333, based on qualifications and experience. Complete tax-free maintenance at nominal costs. For more information write: Superintendent Undercliff Mental Health Center, Meriden, Connecticut 06450.

ASSOCIATE RADIOLOGIST—N.E. Connecticut. 180 Bed Community Hospital. Near large State University. 50% Medical Staff Board Certified Specialist. Moving to new 9 room Department near future. Early partnership. Locums accepted until position is filled. E. Herbert, M.D., Windham Community Memorial Hospital, Willimantic, Connecticut.

ANYONE INTERESTED IN THE ABOVE IS ASKED TO CONTACT THE PHYSICIANS PLACEMENT SERVICE, 160 ST. RONAN ST., NEW HAVEN, CONNECTICUT 06511.

LAW—MEDICINE NOTES

J. Alfred Fabro, M.D.

Res Ipsa Loquitur (Ybarra v. Spangard)

This 1944 Supreme Court of California case is still widely quoted as authority for explaining the doctrine of res ipsa loquitur (the thing speaks for itself) in medical malpractice.

The plaintiff had a routine appendectomy for acute appendicitis. When he recovered from anesthesia (general), he noticed sharp pain in his neck and shoulder, pain he never had before. It continued. Gradually over months he developed permanent partial paralysis with atrophy of the shoulder muscles.

Not knowing who in particular was responsible for the injury, he sued everyone involved in the operation, invoking the doctrine of res ipsa loquitur. Practically, this means that the injury is so obvious that even a layman can infer that it would not have occurred without negligence by someone.

In the ordinary malpractice case, a plaintiff must produce expert medical testimony to prove that negligence by the defendant was the cause of his injury. If he is permitted to invoke the doctrine of res ipsa, however, a decision to be made by the judge, he does not have to get physicians to testify to that effect for him against the defendant. So ordinarily if a plaintiff is unable to get expert medical testimony, the judge may enter a judgment of nonsuit, that is "throw the case out," without the defendant physician's even having to answer the charges. The legal requirement that a plaintiff must have expert medical testimony is an advantage to physicians being sued. Res ipsa, if permitted by the judge, eliminates the need by a suer for expert medical testimony—a disadvantage to a physician being sued.

Res ipsa is a judge-made rule, its use varying from state to state. Some judges, believing that there is a conspiracy among physicians not to testify for plaintiffs even though there seem to be legitimate reasons to sue, permit use of the doctrine by a plaintiff to overcome this so-called conspiracy of silence so that he need not get a physician to testify.

The trial judge in this case entered a judgment of nonsuit against the plaintiff. On appeal, however, the California Supreme Court held that this was an error, that the plaintiff was justified in invoking the doctrine of res ipsa loquitur; and that without the aid of this doctrine a patient who received permanent injuries of a serious character while unconscious from anesthesia while on the operating table, obviously the result of someone's negligence, would be entirely unable to recover unless the doctors and nurses in attendance voluntarily chose to disclose the identity of the negligent person and the facts establishing liability. The doctrine serves to correct such gross injustices.

The court returned the case to the lower court for a new trial, stating: "Where a plaintiff receives unusual injuries while unconscious and in the course of medical treatment, all those defendants who had any control over his body or the instrumentalities which might have caused the injuries may properly be called upon to meet the inference of negligence by giving an explanation of their conduct."

In the retrial, the plaintiff, being able to use res ipsa, did not have to produce expert medical testimony to prove negligence. A judgment was rendered against all the defendants because they were unable, or unwilling, to explain.

As stated by our Connecticut Supreme Court of Errors: "It is a convenient formula for saying that a plaintiff may, in some cases, sustain the burden of proving that the defendant was more probably negligent than not, by showing how the accident occurred, without offering any evidence to show why it occurred."

In the Ybarra case, the patient was unconscious and completely under the control of the doctors. He recovered from anesthesia with an injury not ordinarily occurring after an appendectomy. The injury was far from the field of operation. All the instrumentalities which might have caused the injury were under the control of the defendants. All these facts and conditions taken together implied some negligence, even to the layman, so that no expert medical testimony was required by the plaintiff. It thereby became necessary for the defendants to explain why the injury occurred, and to negate any

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DR. J. ALFRED FABRO, Senior Attending Surgical Staff of the Charlotte Hungerford Hospital, Torrington, Conn.

inference that the injury was due to their negligence.

Whether or not this doctrine is permitted by judges varies from state to state. In some states they are reluctant to permit its use. California is very liberal in its use. But the situation as to malpractice and res ipsa became so bad in Alaska that its legislature passed a statute prohibiting its use by the judges in its state. Res ipsa loquitur is one of the problems facing physicians in the malpractice problem.

Welcome, New Members

Hartford County

Anthony F. Anastasi, M.D., 21 Woodland Street, Hartford, Conn. 06105.

Ara D. Bagdasarian, M.D., 105 Woodland Street, Bristol, Conn. 06010.

Joseph A. Bailey, III, M.D., 2 Holcomb Street, Hartford, Conn. 06112.

Richard H. Bailey, M.D., 1 American Row, Hartford, Conn. 06103.

Jack N. Blechner, M.D., Un. Ct. Sch. of Med., Hartford, Conn. 06115.

Bruce E. Burnham, M.D., 140 Retreat Avenue, Hartford, Conn. 06106.

John A. D'Alotto, M.D., 111 Gillett Street, Hartford, Conn. 06105.

James A. Danigelis, M.D., 477 Connecticut Boulevard, East Hartford, Conn. 06108.

Stephen J. Doctoroff, M.D., 300 Kensington Avenue, New Britain, Conn. 06050.

Herbert J. Douglas, M.D., Bradley Memorial Hospital, Southington, Conn. 06489.

Robert W. Drury, M.D., 2900 Main Street, Glastonbury, Conn. 06033.

Alfonso R. Enriquez, M.D., 300 Kensington Avenue, New Britain, Conn. 06051.

John M. Gibbons, Jr., M.D., 114 Woodland Street, Hartford, Conn. 06105.

Thomas J. Halligan, Jr., M.D., 206 Ashley Street, Hartford, Conn. 06105.

Daniel A. Hart, M.D., Bradley Memorial Hosp., Southington, Conn. 06489.

Howard G. Iger, M.D., 200 Retreat Avenue, Hartford, Conn. 06103.

James J. Jacobson, M.D., 40 Hart Street, New Britain, Conn. 06052.

Lawrence W. Koch, M.D., 320 New Britain Road, Kensington, Conn. 06037.

Bernard Kosto, M.D., 124 Jefferson Street, Hartford, Conn. 06103.

William A. Lynch, M.D., 85 Jefferson Street, Hartford, Conn. 06103.

Robert E. Mueller, M.D., 85 Jefferson Street, Hartford, Conn. 06103.

Rodger K. Nelson, M.D., 300 Kensington Avenue, New Britain, Conn. 06050.

Jose M. Perez, M.D., 73 Cedar Street, New Britain, Conn. 06052.

Lawrence N. Rappaport, M.D., 300 Main Street, Bristol, Conn. 06010.

Jack E. Rosenberg, M.D., 400 Washington Street, Hartford, Conn. 06106.

Donald W. Samson, M.D., 300 Kensington Avenue, New Britain, Conn. 06051.

George D. Sheehan, M.D., 1039 Asylum Avenue, Hartford, Conn. 06105.

Humberto Solano, M.D., 300 Main Street, New Britain, Conn. 06051.

Peter T. Taylor, M.D., 85 Jefferson Street, Hartford, Conn. 06103.

C. Wendell Wickeraham, III, M.D., 353 Center Street, Manchester, Conn. 06040.

Marvin Zelman, M.D., 85 Jefferson Street, Hartford, Conn. 06103.

Arnold S. Zentner, M.D., 854 Farmington Avenue, West Hartford, Conn. 06119.

Doctor's Office

Charles S. Culotta, M.D. announces his retirement from the practice of pediatrics as of November 1, 1970 and that his office at 291 Whitney Ave., New Haven, is being taken over by Marcel Bratu, M.D.

Marvin F. Mankowitz, M.D. announces the opening of an office for the practice of psychology at 5900 Main Street, Trumbull.

Richard W. Munch, M.D. announces the opening of offices for the practice of urology at 24 Church Street, Torrington and 71 Spencer Street, Winsted.

Stephen G. Romeo, M.D. announces the opening of an office for the practice of dermatology at 191 Main Street, Manchester.

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Section of Chest Diseases

Yale-New Haven Medical Center

Arnold B. Rilance, M.D., Director, Winchester Chest Clinics

L.S. #13-58-92, a 64 year old white male, was admitted to Yale-New Haven Hospital on 5/13/70.

Chief Complaints:

Dyspnea, 30 pound weight loss and hemoptysis. An insidious onset in 1969 with gradual weight loss, fatigue, malaise. One week prior to admission he noticed a cough with yellowish, blood streaked sputum. Right sided pleuritic chest pain was of short duration.

Past Medical History:

and review of systems was not pertinent.

Physical Examination:

The patient was emaciated. A localized area of moderate egophony was heard medial to the right scapula. The liver was felt 3 cm. below the R.M.C. The remainder of the physical examination was normal.

Laboratory Studies:

Moderate anemia. Sputum culture—normal flora. Sputum for AFB—negative × 3. Blood cultures × 2—negative. Skin tests: PPD negative.

Sputum cytology—positive for malignant cells consistent with epidermoid Ca.

Pleural fluid—no growth.

Arterial blood bases—pH 7.44; P_{co_2} 31; P_{o_2} 84; Sat. O_2 95.8%.

Course in Hospital:

A diagnosis of carcinoma of the right lung was made. On 6/2/70 the right hemithorax was explored. The tumor was found to be invading the right hilum. A palliative pneumonectomy was then performed. The pathological specimen revealed a lung weighing 550 grams, extensively infiltrated with poorly differentiated epidermoid carcinoma involving the right main and right lower lobe bronchi. The right pulmonary artery was nearly obliterated by tumor.

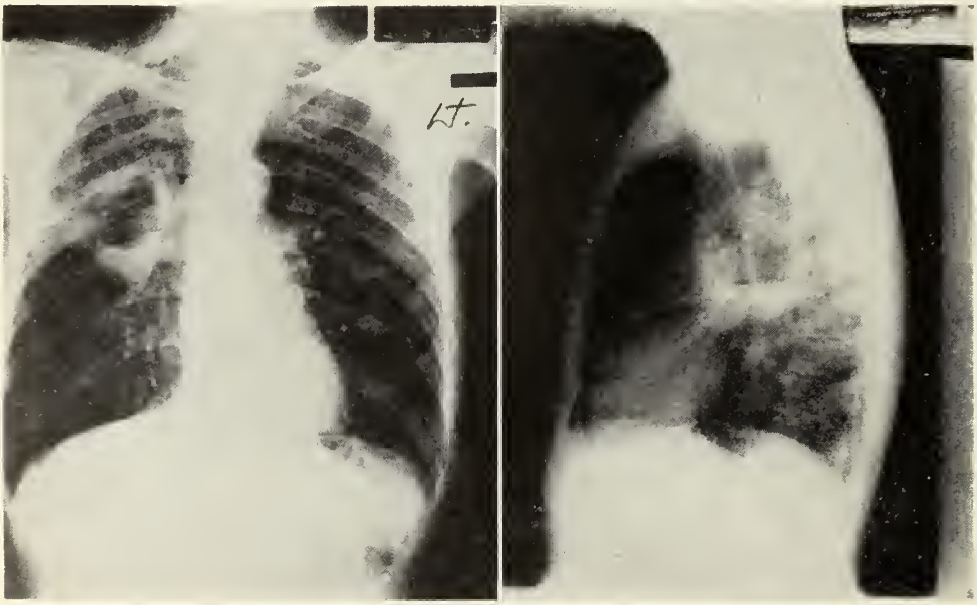

Figure 1

Infiltration of the posterior and apical segments of right upper lobe with a large fluid containing cavity. Note extension into the right hilum and apical segment of the lower lobe.

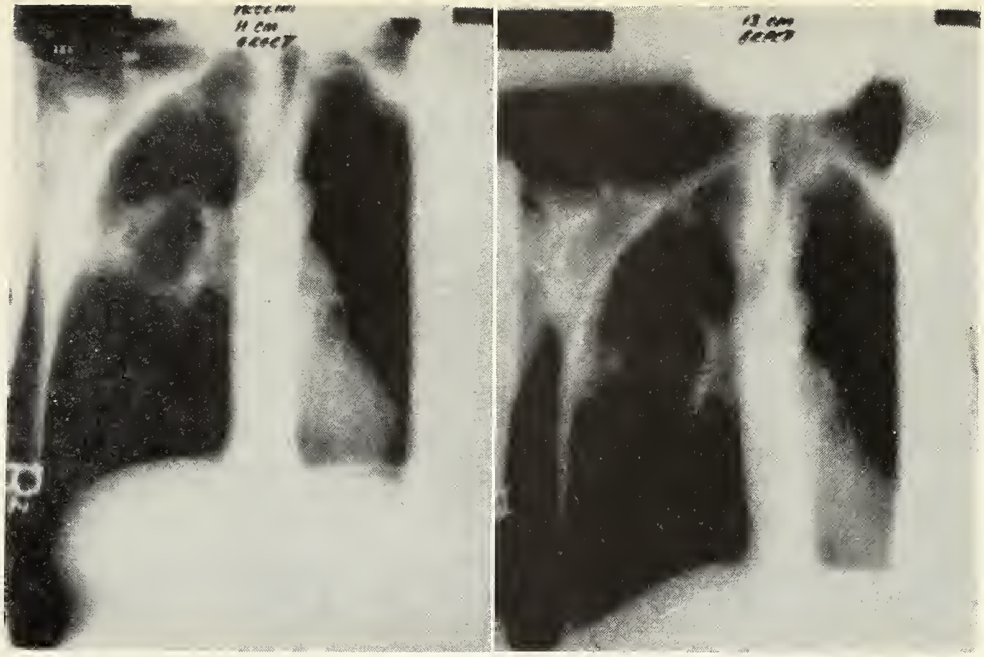

Figure 2

Laminagrams of right lung demonstrating a large cavity with variations in thickness of cavity wall and areas of projecting intra-luminal tumor. This latter finding is most characteristic of an excavating carcinoma of the lung in contrast to the appearance usually seen in a chronic lung abcess. Both the character of the cavity wall and its extension across the major fissure to involve both the upper and lower lobes is an important point in the differential diagnosis.

Members of the Connecticut State Medical Society reading papers before other organizations are requested to submit their papers to the JOURNAL for consideration by the Board of Editors for publication. Please send them to:

Louis H. Nahum, M.D., *Editor*
CONNECTICUT MEDICINE
160 St. Ronan Street
New Haven, Connecticut 06511

Electrocardiogram of the Month: P-waves

Yale-New Haven Hospital
New Haven, Connecticut

Prepared by
HYMAN M. CHERNOFF, M.D.
Associate Professor of Clinical Medicine,
Yale School of Medicine
Director, Dept. of Electrocardiography
Memorial Unit, Yale-New Haven Hospital

In the normal subject P-waves appear upright in leads 1, 2, aVF, and in leads V2 through V6, and inverted in lead aVR. The P-wave may be upright, biphasic, or inverted in lead V1, and in lead 3. When it is biphasic in lead V1 its negative phase does not exceed its positive phase in amplitude or duration. The mean frontal P-axis usually falls in the range of plus 40 to plus 55 degrees and, therefore, the P-wave usually is tallest in lead 2. Its amplitude normaly does not exceed 2.5 mm. in any lead, and usually is less than 2.0 mm. The duration of the P-wave may vary from 0.06 to 0.12 sec. The initial portion of the P-wave represents mainly the depolarization of the right atrium, while its terminal portion represents mainly the depolarization of the left atrium. In body surface scalar leads little or no notching or slurring is observed in the limbs of the P-wave. In the chest leads the P-waves may normally be bifid (M-shaped) but the duration of such P-waves is not prolonged.

The amplitude of the P-waves of normal subjects may vary with changes in heart rate, increasing as the rate increases, as shown in Fig. 1. In the presence of right atrial enlargement, tall peaked P-waves, 2.5 mm. or more in amplitude, may occur in leads 2, 3, aVF and at times in leads V1 and V2. These tall P-waves are usually of normal duration. They are often referred to as P-pulmonale. Such P-waves are seen in Fig. 2, obtained from a patient with right atrial enlargement secondary to pulmonic stenosis, and in Fig. 3, obtained from a patient with advanced emphysema. Similar peaking of the P-waves may be noted during an acute attack of asthma or in other disease states associated with reduced arterial oxygen saturation. The peaking may subside folowing improvement in the patient's ventilation. The finding of peaked P-waves cannot, therefore, be considered as diagnostic of right atrial hypertrophy, but more likely results from dilatation of this chamber, a potentially reversible phenomenon. Fig. 4A and 4B exhibit such changes in P-wave amplitude in a patient during and after an attack of asthma. On occasion similarly peaked P-waves may be seen in normal thin patients. P-waves with a duration above 0.12 sec. are usually associated with left atrial enlargment. They become widely notched (bifid) with the terminal portion, derived from left atrial potentials, exceeding the initial portion both in amplitude and duration. This type of P-wave (often referred to as P-mitrale) is found in mitral valvular disease with overloading of the left atrium, and in some cases of systemic hypertension, aortic stenosis, and following acute myocardial infarction with papillary muscle dysfunction. Fig. 5 exhibits such abnormal P-waves obtained from a patient with rheumatic mitral stenosis. Note the prolonged negative phase of the P-wave in lead V1.

Similar bifid and prolonged P-waves can also be found in patients with advanced coronary artery disease even in the absence of left atrial enlargement. These changes probably result from impaired intra-artrial conduction due to degenerative changes in the atrial myocardium with resultant delay in depolarization of the left atrium. The finding of a prolonged notched P-wave, therefore, cannot be considered as diagnostic of left atrial enlargement alone. Such P-waves should more properly be considered as evidence of a left atrial abnormality.

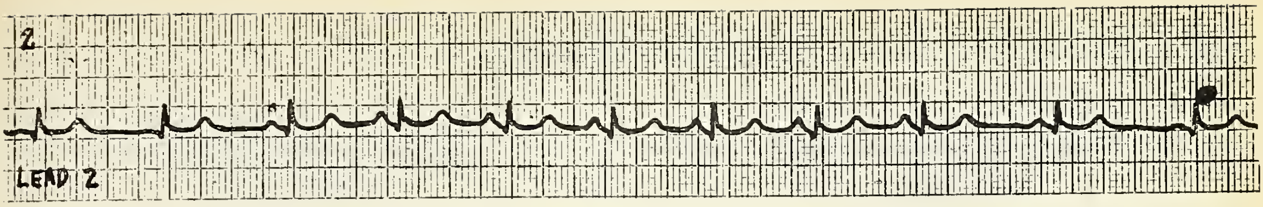

FIG. 1

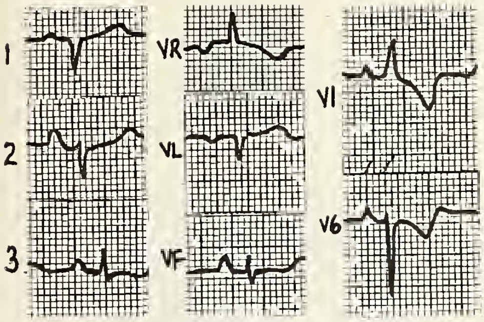

FIG. 2

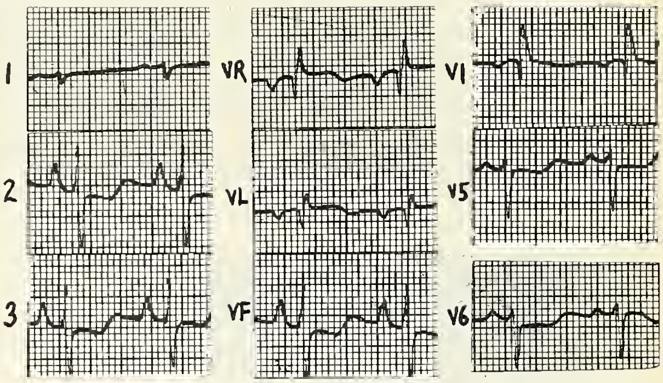

FIG. 3

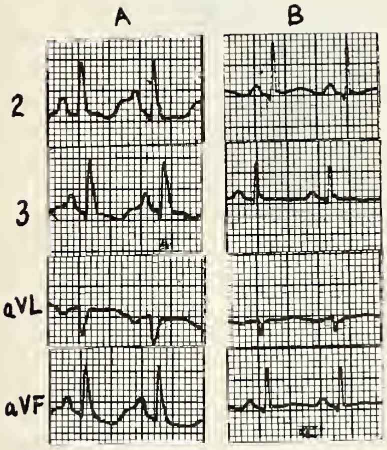

FIG. 4

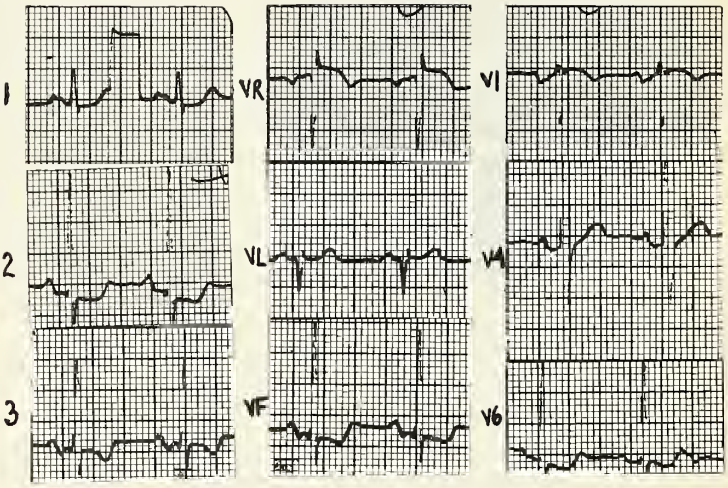

FIG. 5

OBITUARIES

Louis Antupit, M.D.
1895-1970

Dr. Louis Antupit, a physician and surgeon in the Hartford area since 1926. He was born in Hartford on October 24, 1895 and attended local schools. Dr. Antupit earned his B.A. at Trinity College and an M.D. from Jefferson Medical School. He interned at St. Francis Hospital and studied at the Mayo Clinic and Johns Hopkins Hospital.

Dr. Antupit was an Army Veteran of World War I. He was a senior attending physician in surgery at Mt. Sinai Hospital, a member of the staff at St. Francis Hospital and a member of the courtesy staff at Hartford Hospital. He was a former secretary of the Hartford Medical Society, the Connecticut State Medical Society and the American College of Physicians and Surgeons, a Fellow of the American College of Physicians and Surgeons and honorary member of the Medical Fraternity Alpha Omega Alpha and chairman of the Connecticut Alumni Association of Jefferson Medical College. Further affiliations were, Board of Trustees of Temple Beth Israel; the Hartford Jewish Federation; B'nai Brith and the Masons.

Dr. Antupit died on August 1, 1970 after a short illness. He is survived by his wife Sylvia, a daughter Frances of Boston, a son Samuel of Pound Ridge, New York N.Y., five grandchildren and five sisters.

Myron M. Radom, M.D.

Robert R. Nesbit, M.D.
1903-1970

Robert Raymond Nesbit, Chief Pathologist of the Hospital of St. Raphael, died September 20, 1970 in the hospital that he loved and had served so well since 1932.

Dr. Nesbit was born in Pittsfield, Massachusetts, April 24, 1903. In the public schools of that city he received his early education. He was awarded his A.B. degree from the College of the Holy Cross in 1925 and his M.D. from Albany Medical School in 1929.

Postgraduate training, begun in obstetrics and gynecology under the late Dr. J. A. Sampson, pioneer in the study of endometriosis, engendered a desire to pursue pathology in greater depth. As a Littauer Fellow in Pathology at the Harvard Medical School under Dr. Shields Warren, Dr. Nesbit turned toward his definitive career. When, in 1932, Dr. William F. Verdi sought for the Hospital of St. Raphael the best available young clinical pathologist, particularly well oriented in surgical pathology, Dr. Warren recommended his protege, Bob Nesbit. So began a lifetime association between the young pathologist and the young hospital. The growth of both to the highest standards of excellence is now history. The role that Bob Nesbit played in the Hospital of St. Raphael's achievements is known to many, but probably fully appreciated by relatively few.

Dr. Nesbit was a humble, modest, deeply religious man. His contributions to pathology, the clinical services, patient care, the education of countless interns, residents, nurses, medical technologists and others can scarcely be fully grasped. Generations of former students and later colleagues, however, came to recognize in him a bulwark in their lives, a truly inspirational human being and a most valued friend.

With a great gift for planning and design Bob was equally at home with drawing board or carpenters tools. Architects, carpenters, plumbers, electricians, policemen and lawyers shared with him work experiences and relationships at least as closely as did his medical colleagues. Bob's gifts for relating to his fellow man and a keen sense of humor endeared him to all. An abiding faith in men of all stations and creeds earned for him universal respect.

Diplomate of the American Board of Pathology he was a member, fellow or past president of many related professional and service organizations.

Dr. Nesbit never swerved from his devotion to the values he placed highest—his God, his Catholic faith, the Hospital of St. Raphael, his home and his beloved family. Surviving him are his widow, Helen Mahar Nesbit, his daughter, Nancy Nesbit Brigham, his son Robert R. Nesbit, Jr., M.D., two sisters and five especially cherished grandchildren.

Bernard F. Mann, Jr., M.D.

In Memoriam

De Angelis, Louis R., Medical College of Virginia, 1936. Dr. De Angelis was a general practitioner in the New London area since 1937. He was a member of the American Academy of General Practice, the American Geriatric Society, the New London County Medical Association, the Connecticut State Medical Society, and the American Medical Association. He died October 2, 1970, at the age of 66.

Drake, Leo Berthier, Harvard Medical School, 1923. Dr. Drake was retired and residing in Sarasota, Florida, at the time of his death. He was a member of the American College of Chest Psysicians, the Hartford County Medical Association, The Connecticut State Medical Society, and the American Medical Association. Dr. Drake died September 15, 1970, at the age of 73.

Friery, Clarence Milton, Sr., Boston University, 1929. Dr. Friery was a general practitioner in the Hartford area since 1929. A former president of the Hartford County Academy of General Practice, Dr. Friery was also a member of the Hartford County Medical Society, the Connecticut State Medical Society, the American Medical Association, the Hartford County Academy of General Practice and the American Academy of General Practitioners. He died September 10, 1970, at the age of 68.

Karpel, Saul, University of Maryland, 1936. Dr. Karpel specialized in internal medicine in the New London area since 1946. He served in the U.S. Army from 1941 to 1946, and was senior attending physician at Lawrence & Memorial Hospital. Dr. Karpel was a member of the New London County Medical Society, the Connecticut State Medical Society, and the American Medical Association. He was 60 at the time of his death.

Kligerman, Martin James, Yale Medical School, 1964. Dr. Kligerman was a psychiatrist in the New Haven area since 1966. He was a First Lieutenant in the U.S. Army Reserve from 1962 to 1968, and was a resident physician at the V.A. Hospital in West Haven Conn. Dr. Kligerman was a member of the New Haven County Medical Association, the Connecticut State Medical Society, and the American Medical Association. He died September 16, 1970, at the age of 34.

Meyer, Fritz Martin, Indiana University School of Medicine, 1928. Dr. Meyer was a pediatrician in the Bridgeport area since 1928. He was attending pediatrician at Bridgeport and St. Vincent's Hospitals. In 1962 he was appointed an assistant medical director for the Connecticut State Welfare Department. Dr. Meyer was also a member of the Fairfield County Medical Society, Connecticut State Medical Society and the American Medical Association. He died August 23, 1970 at the age of 70.

Priddy, Foster Eugene, Northwestern University, 1928. Dr. Priddy was a practicing physician in the Vernon area since 1930. Dr. Priddy served overseas during World War I with the Second Army Division. In November, 1930, he became the first full-time physician at Connecticut State Prison in Wethersfield, and at the same time had a private practice from 1932-1957 in Hartford. Dr. Priddy was a member of the American Medical Association, Hartford Medical Society, Hartford County Medical Society, Connecticut State Medical Society and the American Prison Association. He died August 24, 1970 at the age of 74.

WOMAN'S AUXILIARY

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Mrs. Edwin R. Connors, Pawcatuck

Six state Auxiliary Board members attended a national workshop held on October 3rd and 4th in Philadelphia. Conferences started at 8:00 A.M. and ran over into the evening.

Following are some notes from the different conferences:

AMA-ERF: Woman's Auxiliary contributions to AMA-ERF for 1969-1970 totaled $498,950.60 — a phenomenal $70,074.92 increase over the preceding year's contribution. Once again auxiliary members have pledged their support to two of the foundation's most important projects—The Fund for Medical Schools and the Student Loan Guarantee Program. AMA-ERF's Fund for Medical Schools helps relieve the financial problems facing every medical school dean in this country. Not only are normal costs of operation mounting, but in order to meet the additional demands for more physicians, medical schools must expand their enrollments. AMA-ERF's Student Loan Guarantee Program helps the individual student. Since there is no predicted relief in student loans from the federal government, we must increase available AMA-ERF funds to help many young students, interns and residents.

COMMUNITY HEALTH: This year the AMA has asked that we emphasize *Blood Donor Recruitment* and *Physical Fitness for Adults.* Also, we hope that we might take "a giant step for mankind, by rubbing out Rubella," a menace to the unborn. By sponsoring a *Community Health Week,* these requests may be given greater attention. Preparing for such a program takes time and is best done by combining forces with your medical society. Also, you are urged to invite other community groups to participate.

HEALTH CAREERS: Our goal in Health Manpower is to recruit Ten Percent of all high school graduates for the 200 health-related occupations. Recruitment must include the coordination of the efforts of the medical auxiliary to blend into the network of recruitment activities of medical societies, educational institutions (public schools, vocational-technical schools, junior and community colleges and universities), hospitals, professional societies and auxiliaries, service organizations, American Legion, etc.

1. Make available comprehensive and detailed information pertaining to education, training, duties and supply of every professional, technical and auxiliary health worker.
2. Promote health careers clubs in high schools (help furnish programs and field trips).
3. Improve counseling by guidance counselors, science teachers and career professionals.
4. Help the inactive and retired health worker to get back into service with refresher courses.
5. Expand work study programs in vocational schools.

MEMBERSHIP: GOAL!

Every doctor's wife an auxiliary member.

a. Retain the present members.
b. Rescue the dropouts.
c. Recruit the reluctant.

HOW?

Provide the challenge of:

a. Closer liaison with county medical societies' activities and developments. b. Overcome complacency and indifference by providing meaningful, productive, related programs to enlist and maintain the interest of doctors' wives. c. Active leadership and recruitment by officers, regional vice-presidents, and chairmen of national, state and county societies, utilizing prepared packets, personal contact and camaraderie. d. Be informed and persuasive in competing for the interest, time, services and efforts of doctors' wives in developing our input to the health care system and community life.

From the

Connecticut Regional Medical Program

Henry T. Clark Jr., M.D., Director

A major focus of CRMP's activities is to provide improved access to the expanding body of medical literature and effective library services to physicians and allied health workers in their communities. The Regional Library Services program, operational some 16 months, works toward that objective through document delivery to requesting physicians and other professionals and consultation and training of hospital library personnel.

At present the Regional Library Services is filling requests at the rate of 10,000 pages per year, roughly equivalent to 2.5 per practicing physician. The training program consists of one-day workshops at Yale and at The University of Connecticut on all phases of medical library operations monthly from October through May.

Vernon Lippard, M.D., Chairman of the Regional Library Services' Technical Advisory Committee, reported on the development of the program at the September meeting of the CRMP Advisory Board. He is a former Dean of the Yale Medical School and a founding member of CRMP.

In his remarks, Dr. Lippard said the committee which he heads is an outgrowth of CRMP Planning Task Force 7, which conducted a survey during 1967 that illustrated hospital libraries, with rare exceptions "were in a deplorable state of underdevelopment." On that basis, he added, there seemed to be little hope of establishing an effective program of continuing education until that basic resource was developed.

It was also apparent from the outset that hospitals needed more than prodding, they needed some professional guidance, Dr. Lippard stated, "In this connection the Program was very fortunate in obtaining the services of Mr. John Timour, a former staff member of the National Library of Medicine, who joined the staff of CRMP on July 15, 1969. At that same time the Technical Advisory Committee was organized and held its first meeting in September, 1969. The Committee felt that the development of quality library service required two approaches: 1) the establishment and/or improvement of libraries in all of the general and special hospitals in the state; and 2) the development of supporting services."

It was found that, as a first step, the hospitals needed guidance as to what is a reasonable expectation in terms of space, staff and collections, according to Dr. Lippard. Consequently, guidelines, stated in comparatively simple form, were developed for hospitals of various sizes, setting forth reasonable expectations and standards. "After these guidelines were widely circulated in the spring of 1970, Mr. Timour conducted a survey to find out how existing libraries measured up to these minimal standards," he said.

"The results were quite disappointing: on a scale of 100, the average hospital rated about 60. The results of the survey were reported on a confidential basis; each hospital now knows where it stands. One of the surprising discoveries, however, was how little it costs to operate a good, efficient, adequate library in a hospital." For example, Dr. Lippard told the Advisory Board members, the minimum annual operating budget for staff, books, and journals in a hospital of up to 200 beds would come to only $4,800; for a 200-400 bed hospital the sum would be only $11,000 and for a 400-600 bed hospital $15,000. "When related to total hospital budgets, these sums are small, indeed."

As for the development of supporting services, the objective was to have available to every health worker, at no cost and fairly promptly, any medical literature available in the world. This objective was achieved, first, by establishing a WATS (Wide Area Telephone System) service—which means one can telephone toll-free from any hospital library to the Yale or University of Connecticut Medical Libraries.

Second, according to Dr. Lippard, a TWX (Teletype) system was installed so that the medical school libraries can forward requests they cannot meet to the Regional Medical Library in Boston and to the National Medical Library in Washington. "As a result of this prompt service and the availability of free photocopies of literature, the demand for this service has grown very rapidly. With special personnel in each of the two libraries paid by this program this material has been mailed promptly. As a consequence, during the first year, requests for this service have grown three times."

Dr. Lippard continued: "Through the CRMP supplemental grant (of April 30, 1970) it was possible, as of September, to employ reference librarians assigned to Yale and to the University of Connecticut. It is now possible for the local hospital library to call upon these reference librarians to do a complete search of the literature. As a result, also, of this grant a user study is being carried out in selected urban and rural areas to determine what the users want. In addition, a program is underway to combine the two hospital libraries in Stamford—those at St. Joseph's and Stamford Hospitals. The objective is to consolidate their resources for greater effectiveness and efficiency of operation."

Looking to the future, Dr. Lippard visualized the hospital library as essential for the foundation of good medical education for interns, residents, clinical clerks and allied health personnel. More important, it is needed to carry on continuing education programs for physicians. Although the program has been under way for only a year, a great deal of interest has been generated. It now remains for local hospital staffs and administrators to provide the space, the staff, and the facilities to develop their library resources. He stated that support for this kind of program should appeal to women's auxiliaries, for example, since it has a modest budget and the results are tangible.

Finally, if the momentum gained in the past year is to be maintained, and there are to be results from this effort, the Connecticut Regional Medical Program should continue its support of this program for another year or two, Dr. Lippard concluded. After that the basic program should have established itself and the program should be self financing.

AROUND THE STATE

NEW HAVEN COUNTY

Board of Governors

New Haven County Medical Association

The Board of Governors of the New Haven County Medical Association met on Thursday, September 17, 1970 at the Waterbury Club in Waterbury with President Stewart J. Petrie, M.D. presiding.

Dr. Petrie reported that during the summer he attended two health planning meetings and held a leadership conference with each of the local society presidents or vice-presidents. At this meeting at least one member from each of the five local geographical societies were present thusly guaranteeing full local participation. Plans and programs as well as problems that are of mutual concern were discussed.

New Haven County has arranged for the Public Affairs Division Teams to come to the Milford, Naugatuck Valley, New Haven and West Shore (Milford) local areas to demonstrate how grass roots physician participation in political and legislative matters can be developed.

The proposed budget and dues increase was revised and approved for submission to the membership at the semi-annual meeting.

Dr. Cappucci reported that the Public Relations Committee with the aid of the Public Relations Director, Mr. Arthur Schuman has instituted the following programs:

1. A President's Newsletter to the membership is published monthly.
2. A Speakers Bureau with over 60 participants has been formed.
3. A quarterly Journal to inform the membership with Dr. James Root, Jr. as Editor is being published.
4. Local radio programs are being developed for each local area.
5. Planning is now under way for the development of a news release program in the available media.

Councilor Kurt Pelz reported that the Connecticut State Medical Society's President, Dr. Morris Granoff, has nominated Dr. Franklin Robinson for appointment by Governor Dempsey to the Connecticut State Medical Examining Board.

Dr. Pelz reported that the Connecticut State Medical Society is working diligently on the problem of malpractice insurance costs and hopes to have an optimistic report in the near future.

Because of the ever-broadening scope and complexities of "Health Planning" it was voted to form a new committee to be called the Health Planning Coordinating Committee. This committee will attempt to obtain a better understanding of the subject followed by a more effective participation in health planning by the New Haven County Medical Association.

The rather lengthy meeting heard 18 committee reports and approved them for presentation to the membership at the semi-annual meeting on October 22, 1970.

William L. West, M.D., *Clerk*

Science News

Link Between LSD And Birth Defects Reported

(*JAMA* 212, 1447, June 1, 1970) Dr. Cheston M. Berlin and Cecil B. Jacobson reported that the incidence of defects in children born of parents who take LSD is extremely high. The rate of central nervous defects was about 16 times that in the general population.

The mothers were a very high risk obstetric population for many reasons—multiple drug use (25% used other narcotics), infectious diseases and malnutrition. Most of the mothers also smoked (81%).

One of the findings in all abortion specimens was failure of fusion of the cortex. The fathers of the six abnormal infants admitted to taking LSD before and around the time of conception. Six women LSD users were followed through more than one pregnancy. In each case, the first pregnancy ended in a normal term delivery. "Of eight subsequent pregnancies, four terminated in abnormal fetuses." —L.H.N.

Filtering Blood May Avert Bypass Brain Damage

(*JAMA*. 212, 1450, June 1, 1970) Microparticles formed in blood after passage through a pump oxygenator caused a significant depression in brain metabolism that was not immediately reversible. These particles now can be screened out according to Brennan. Patterson and Kessler.

One report said 53 of 100 patients studied showed cerebral disturbances during the postoperative period. Others have linked brain damage after open-heart surgery to lack of adequate blood flow to the brain.

The animal experiments by the Brennan group from Cornell were designed to investigate the nature and extent of brain damage during bypass and whether a filter to eliminate the microparticles would minimize the effects. The filtered group of animals all escaped cerebral injury.—L.H.N.

Fixed Combination Drugs

(*Science*. 169, 262, July 17, 1970). The FDA has ordered off the market 48 drugs containing fixed combinations of penicillin and sulfa and penicillin and streptomycin.

The FDA first published an order to halt marketing of these drugs in June 1969, but appeals by the drug companies delayed action on the order for a year.—L.H.N.

Circadian Rhythms in Human Heart Homograft

(*Science* 169: 694, August 14, 1970, Kraft, I. A., et al) The authors recorded the electrocardiogram and cardiotachogram of a patient with a human heart transplant over a period of 72 hours. Within the donor P-QRS-T complex one can identify the P waves emanating from residual sinoatrial tissue of the recipient.

The recipient P waves are independent of the donor complexes.

A clear circadian rhythm (23.4 hours) in heart rate is maintained in both donor and recipient tissue, the donor complexes preceding by a phase shift of 135 minutes the complexes of the recipient heart tissue. Both tissues display clear morning and evening maximum rates paralleling activity and lighting cycles.—L.H.N.

New GRAS List

(*Nature*. 226. 309, April 25, 1970) The FDA asked that food manufacturers in the U.S. using food additives licensed in 1958 should reapply to have these included in the list of materials generally recognized as safe (GRAS).

An official of the FDA explained that when the present formal procedures for including materials on the GRAS list were introduced in 1958, a large number of compounds used with food additives have been approved on the basis of advice of variable quality and in comparatively informal ways.

What has happened now is that food manufacturers have been asked to reapply for the inclusion in the GRAS list of food additives originally approved before 1958. The FDA has undertaken to give some kind of an answer within 30 days.

By all accounts it does not know how many compounds will be affected—it may be anything between 1000 and 10,000. Much will depend on the extent to which previous permissions are subsumed in later more formal approvals.—L.H.N.

Saccharin Passes Latest test: Ordinary Use Deemed Safe

(*J.A.M.A.* 213 118 August 17, 1970). Saccharin poses no hazard in the quantities in which it is likely to be used, a National Academy of Sciences-National Research Council Committee has told to FDA.

A "safe" level for men is about 5mg/kg/day or 12 to 18 quartergrain tablets per day.

"Tests for carcinogenic effects by applying saccharin to the skin by subcutaneous injection, or by implanting pellets into the bladder have no known relevance to the safety of saccharin consumed orally" the report said.

The 80 year history of saccharin use by man without evidence of adverse effects except for rare cases of photosensitization should be given due consideration in the overall toxicologic evaluation, the panel said in its report.

A recent cancer mortality study in more than 21,000 diabetics showed no increase risk of cancer including that of the bladder during the period 1931-1959. "It is unlikely that even gross misuse of saccharin over a short period of time would be hazardous."

The NAS-NRC panel recommended further investigation into the long-term effects of saccharin in at least two animal species; epidemiologic factors, particularly in diabetes, patterns of saccharin-sweetened foods stored under a variety of conditions; and the toxic interaction between saccharin and other substances.—L.H.N.

Cell-Mediated Immunity Shown by Lymphocytes From the Respiratory Tract

(*Science* 169: 696, August 14, 1970, Henney, C. S., Waldman, R. H.) Lymphoid cells of the respiratory tract can produce antibody after antigenic stimulation. In this report lymphoid cells which were obtained from the washings of animals immunized with antigen in nose drops, exhibit a characteristic cell-mediated immunity in that they specifically prevent macrophage migration in the presence of antigen. Splenic lymphocytes from these animals do not cause such inhibition. The converse is true of animals immunized parenterally.

These findings then reveal local induction of cell-mediated immunity in the respiratory tract by local installation of antigen.—L.H.N.

Lymphosarcoma Remission Following Serum Hepatitis

(*J.A.M.A.* 210 1590 November 24, 1969, Lewis R. Weintraub, M.D.) A clinical and hematologic remission associated at onset with the occurrence of serum hepatitis developed in a patient with lymphocytic lymphosarcoma unresponsive to medical therapy.

The case is unique in that the patient did not receive any chemotherapy for five months prior to the viral hepatitis and the subsequent complete remission lasted for 22 months at which time the patient died from another disease, congestive heart failure.

The case supports the growing contention that the production of interferon by one virus may be responsible for the alteration in the course of leukemia and lymphoma.—L.H.N.

Experiences in the Treatment of Paget's Disease of Bone With Mithramycin

(*J.A.M.A.* 213 1153 August 17, 1970, Will G. Ryan, M.D., Theodore B. Schwartz, M.D.; and Gretajo Northrop, M.D., PhD.) The effects of mithramycin an antibiotic with cytotoxic activity, were observed in 15 patients with active Paget's disease of bone.

It had a consistent effect in suppressing the activity of Paget's disease, as reflected by changes in serum alkaline phosphatase and urinary hydroxyproline levels and the occurrence of symptomatic relief. These responses are probably mediated by a cytotoxic effect on osteoclasts.

Several patients have shown prolonged remissions.

This agent shows considerable promise as an effective treatment in the bone disease but means of enhancing the therapeutic: toxicity ratio need further study.

Mithramycin was given to the 15 patients as 8 to 12-hour infusions in a dose of 25μg/kg/day for ten days. All other medications are withheld during the period of treatment with mithramycin to reduce incidence of toxicity in platelet hepatic and renal function.—L.H.N.

Early Arterial Thrombosis Seen In Gout Patients

(*JAMA,* July 27, 1970, 544, 213, No. 4) Persons with primary gout may develop early arterial thrombosis according to Dr. Frank J. Viozzi, based on a study of 280 gout patients.

The incidence of first myocardial infarction in his study as well as the Framingham report was highest in the sixth decade of life, but there was no significant differences between the gout group and the Framingham subjects.

Between the ages of 30-40, 0.5 per cent suffered a myocardial infarction. The incidence among gout patients is 14 times as high.

In the 40-50 year age group, the incidence of heart attacks among gout patients was seven times as great as among ordinary subjects.

Viozzi believes the higher rate of thrombotic disease is related to increased serum uric acid levels.

—L.H.N.

Vision Information Center: A User-Oriented Data Base

(*Science,* 169: 29, July 3, 1970, Eichhorn, M. M., Reinecke, R. D.) In response to the information needs of scientists and physicians who work in the field of vision, these authors have developed a direct-access on-line specialized information retrieval system which combines computer-assisted instruction and bibliographic retrieval. An essential feature of the system is its accessibility via remote computer terminal.

Courses of instruction in selected subjects in ophthalmology have been programmed and form part of the data base.

A search of the literature retrieval system by a single subject or by a combination of several subjects retrieves the appropriate bibliographic citations.

The response to the service offered by the Vision Information Center indicates that the center should expand its facilities to satisfy the needs of its clients.

—L.H.N.

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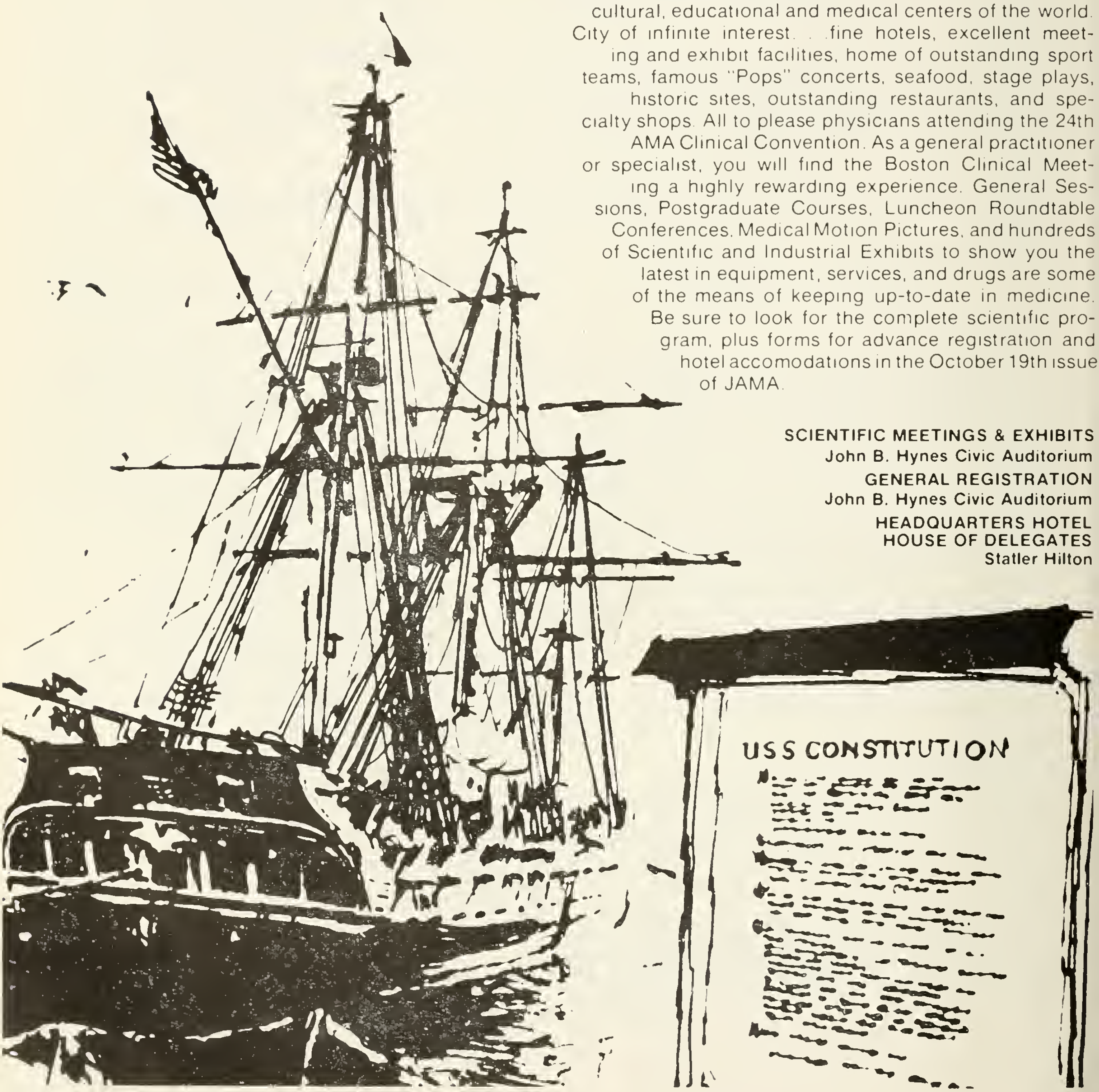

MEETING NOTICES

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GENERAL

April 27-29, 1971—Tuesday-Thursday

Connecticut State Medical Society
179th Annual Meeting of the Connecticut State Medical Society
Hilton Hotel, Hartford, Connecticut

November 29-December 2, 1970
Sunday-Wednesday

AMA 24th Clinical Convention
Boston, Massachusetts

November 29, 1970—Sunday

12th National AMA Conference on the Medical Aspects of Sports
Sheraton-Boston Hotel
Boston, Massachusetts

December 1, 1970—Tuesday—9:00 A.M.-3:30 P.M.

"Lead and Your Environment Conference"
Hartford Medical Society Auditorium
Keynote Speaker: Clair C. Patterson, Ph.D., Senior Research Fellow in Geochemistry, California Institute of Technology
Sponsors: University of Connecticut School of Medicine, Department of Pediatrics; Yale University School of Medicine, Department of Pediatrics; Connecticut Air Conservation Committee; Connecticut State Department of Health.

INTERNAL MEDICINE AND SURGERY

September 15-June 1—Tuesdays

Lecture Series: "Medical Emergencies"
Lawrence and Memorial Hospitals
New London, Connecticut
Contact: Edward Gipstein, M.D., Director of Medical Education. (442-0711 ext. 361).

January 7-9, 1971—Wednesday-Friday

National Conference on Cancer of the Colon and Rectum
Hotel del Coronado, San Diego, California
Contact: American Cancer Society, 219 East 42nd Street, New York, New York 10017.

January 14, 1971—Thursday
Annual Meeting of the Connecticut Chapter American College of Surgeons
Hotel Sonesta, Hartford, Connecticut

ONCOLOGY

December 3, 10, 17, 1970—12:00 Noon-Thursdays
The Hospital of St. Raphael
New Haven, Connecticut

December 3—Metastatic Tumors of Testes and Prostate—Leonard Farber, M.D.

December 10—Case Presentations—Carcinoma of Prostate

December 17—Tumors of the Mediastium—Edwin Neville, M.D.

PSYCHIATRY

November 24, 1970—Tuesday
Lecture: The Distributions of Mental Disorders in Populations: Challenges of Psychiatric Epidemiology
Speaker: Jules V. Coleman, M.D., Clinical Professor of Public Health and Psychiatry, Yale University School of Medicine, Department of Epidemiology and Public Health.
Connecticut Valley Hospital, Merritt Hall Auditorium, Middletown, Conn.

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CONTENTS

The President's Page 837

scientific

Clinical Application Of Atrial Pacing Stress Electrocardiography, *Charles N. Leach, Jr., M.D.* and *Charles E. McLean, M.D.* 839
The Pharmacology Of Immunosuppressive Agents, *Malcolm S. Mitchell, M.D.* and *Joseph R. Bertino, M.D.* 843
Splenectomy As An Adjunct To The Treatment Of Hodgkin's Disease, *Sherwin B. Nuland, M.D.* 851
The Management Of Hodgkin's Disease: Evolution Of Radiotherapy Concepts, *Raul Vera, M.D., Leonard R. Prosnitz, M.D., James J. Fischer, M.D., Ph.D.* and *Morton M. Kligerman, M.D.* 856
The Yale Combination Chemotherapy Program For Advanced Hodgkin's Disease, *Martin Levitt, M.D., Ronald C. DeConti, M.D., Howard A. Pearson, M.D., John C. Marsh, M.D., Robert P. Zanes, Jr., M.D., Malcolm S. Mitchell, M.D., Harvey W. Kaetz, M.D.* and *Joseph R. Bertino, M.D.* 862

editorials

The Outlook For Control Of Acute Respiratory Tract Disease 867
Marihuana: II 871
Calcium Malabsorption With Advancing Age 874
Drug Induced Lupus Erythematosus Syndrome 875
Androgen Function And Impotence 878
Science Tools: Tubeless Gastric Analysis By The Heidelberg Capsule 879
Amantadine In Parkinson's Disease: An Instance Of Medical Serendipity 880
The "Hard" Costs Of Air Pollution 881
The Winter Toll Of Fatal Heart Attacks 882
Continuing Education 883

departments

From the Executive Director's Office 886
Physician's Placement Service 890
Special Articles:
Adverse Effects of LSD: A Current Perspective, *David J. Greenblatt, M.D.* and *Richard I. Shader, M.D.* 895
The Use of Drugs in Various Types of Cancer, *David S. Fischer, M.D.* 903
Electrocardiogram-Of-The Month, *Hyman M. Chernoff, M.D.* 910
X-Ray Of The Month, *Arnold B. Rilance, M.D.* 914
Woman's Auxiliary 915
Around The State 916

miscellaneous

In Memoriam 894
Meeting Notices 919
Science News 920
Connecticut Regional Medical Program 922
Book Reviews 924
Yearly Index . . . . i-vii

THE PRESIDENT'S PAGE

The physician is the product of a continuing educational experience. During his early school years he learns from his teachers and from the text books. This learning experience is in later years extended to include the laboratory and still later, in the clinical and post graduate years, the patient. Following the completion of this formal or more structured education, the physican in practice continues to learn by studying his patients and observing the course of their illnesses and the effects of the treatment he has instituted. This method of continuing education was the one in vogue prior to the present century. It produced some very fine physicians and led to many scientific discoveries. It still has its place in the continuing education of the modern physician. However, it should be only part of that education.

The science of medicine has made gigantic strides in the past fifty years and continues to make similar strides today. The body of medical knowledge continues to increase almost daily. For the physician in practice, to keep abreast of these advances is a monumental task. However he must do so if he is to deliver to his patients the best medical care. Since one of the goals of the Connecticut State Medical Society is to help its members deliver to their patients the best medical care, the problem of continuing education and how to achieve it has long been a concern of your Society.

The need for continuing education was recognized many years ago by the American Academy of General Practice, when on its organization, it required of its members 150 hours of approved study every three years. This guide-line of approximately 50 hours per year is a useful one. This may be achieved by attending the scientific meetings of various medical associations, participating in the educational programs of local hospitals (some of which are excellent) and attending full-time or part-time courses offered by medical school and the staffs of larger hospitals.

At its Clinical Convention in December 1968, the American Medical Association House of Delegates established the "Physician's Recognition Award" for participation in Continuing Medical Education. One of the purposes of the Award is to encourage physicians to participate regularly in continuing medical education. The guide-line used by the AMA for qualification for the award is a minimum of 150 credit hours over a continuous three years period.

At a recent meeting of the Society's Committee on Post-Graduate Education there was a difference of opinion as to whether Continuing Education should be compulsory or voluntary. I favor the voluntary approach and I feel that the Society should help its members obtain the education they need to keep abreast of the advances. Only if the voluntary approach fails would I favor compulsion. However, I recognize that the critics of medical care quality are advocating periodic re-examination (and re-licensure) and recertification for specialists.

The weaknesses of scientific meetings and hospital educational programs lie in the area of not always fulfilling the needs of individual physicians. To overcome this I would recommend a program of self-evaluation by each physician either by submitting to a self-assessment examination or personal deep intropection. Each one who has given some thought to the problem knows where his weaknesses lie. However, even for those, a self-assessment examination could uncover a weakness of which he is unaware. Having ascertained the areas where he needs improvement the individual physician can then develop a program of self-education. The Society could then be in a position to advise as to how or where this could be implemented.

As we all know there are many part-time and full time courses available in many fields. The *JAMA* publishes a voluminous list once a year. In addition the technology of education has made great advances. There are now audio-tapes of excellant scientific quality on a variety of medical subjects and it won't be long before programmed instruction using audio-visual tapes will be available at modest cost. Futhermore, let us not forget the numerous scientific journals and textbooks which are available and which can be used for basic information and as reference sources.

The chief result that will be achieved by a good program of Continuing Education is the elevation of the quality of medical care. However, there are also some fringe benefits. The conscientious physician will also get some personal gratification from the knowledge that he is giving his patients the best care and thus better fulfilling his responsibility to them. Futhermore isn't it conceivable that improving the quality of medical care could have a favorable effect on the malpractice situation.

Many problems today are so complex that they require the expertise and cooperation of people in different but related fields for their solution. This could be applied as well to Continuing Medical Education. A joint effort by organized medicine, medical educators, and hospital staffs and administrators could be very productive. I hope something along these lines will be started soon.

Morris A. Granoff, M.D.

Clinical Application of Atrial Pacing Stress Electrocardiography

Charles N. Leach, Jr., M.D. and Charles E. McLean, M.D.

During the past year, we have encountered several patients with suspected coronary artery disease whom we could not evalute with conventional exercise electrocardiographic techniques. They declined to walk on the treadmill, were too heavy to perform properly, were troubled with claudication, or had other reasons for not exercising. The technique of transvenous atrial pacing, as described by Sowton and Lau offered a method for exercising the myocardium by means of rate stress without requiring exercise effort on the part of the patient.[1, 2]

We chose to employ this technique, and to compare its usefulness with treadmill exercise studies in a group of patients who were also studied by means of selective coronary arteriography. The results are presented in this communication.

Materials and Methods

Twenty-five patients suspected of angina pectoris and ischemic heart disease were studied by the atrial pacing technique. There were four women and twenty-one men. Ages ranged from thirty-four to sixty-six years with a mean of fifty-one. No patient used cardiac medications other than nitroglycerin on the day of study, and no patient had received cardiac glycosides.

A bipolar #6 pacemaker catheter was positioned in the high right atrium in twenty-three cases, and the coronary sinus in two. This was done at the time of coronary arteriography in most cases. In some, the basilic vein was entered through a one-centimeter cutdown which was easily closed with a single suture. The heart was then paced at three primary rates approximating 120, 140, and 160 beats per minute. Serial electrocardiograms were recorded from the limb leads, and the V2, V5, and V6 positions during the second minute of each pacing rate and each minute of a six to eight minute recovery period. Generally, pacing currents of 1.0 to 2.5 ma were used. In no case was more than 5 ma necessary.

Submaximal exercise electrocardiography was performed on a Collins Treadmill using a fixed 10% grade for all walking rates. The patients walked for one to three minutes at 1, 3, and if necessary 4 or 5 miles an hour until a maximal heart rate of at least 160 beats per minute was attained. The exercise was stopped if fatigue, chest pain, or major electrocardiographic changes were noted. The rate of 160 beats was approximately 80% of the rate attained by Lester's subjects at maximal exercise levels.[3] The patients did not rest between exercise stages. Electrocardiograms were recorded with each minute of exercise, and during each of 8 to 10 recovery minutes.

Exercise and atrial pacing electrocardiograms were considered positive if the ST segment was depressed 1 mm. below baseline level and was flat or downsloping. J point and isolated T wave changes were not considered diagnostic.

Selective coronary cine-angiograms were made in the PA, left and right oblique projections of each vessel in seventeen cases. These were reviewed by three observers and graded according to the maximal degree of obstruction visible in any primary or secondary coronary branch. Vessels graded "O" were entirely normal or showed very minor scalloping of their silhouettes but no discrete lesions. One plus lesions narrowed the vessel lumen by up to 25%; 2 plus lesions from 25 to 50%. Fifty to seventy-five per cent obstruction was graded 3 plus, and stenoses of over 75% were graded 4 plus.

Results

Atrial pacing was carried out with ease in all patients in whom it was attempted. The studies were not complicated by arrhythmias except for transient second degree heart block which was easily abolished by intravenous atropine, 0.5 to 1.5 mg. No ill effects resulted from the studies.

Seventeen patients had both atrial pacing and coronary arteriography (Table 1). Six of these had constricting lesions in the 4 plus category. No 3 plus coronary narrowing was found. Four of the six

---

DR. CHARLES N. LEACH, JR., Director, Cardiac Laboratory, New Britain General Hospital, New Britain, Conn.

DR. CHARLES E. McLEAN, Director, Cardiac Laboratory, Hartford Hospital, Hartford, Conn.

Work performed in the Cardiac Laboratory of the Hartford Hospital.

TABLE 1

COMPARISON OF PACING STRESS ELECTROCARDIOGRAPHY WITH CORONARY ANGIOGRAPHY

Pt.	ST Depression	Angina	Greatest Coronary Stenosis				
			0	1+	2+	3+	4+
1	1 mm	Mild					X
2		Mild					X
3		Atypical		X			
4		Severe					X
5		Mild			X		
6		Mild					X
7		Atypical	X				
8	1/2 mm	Atypical	X				
9		Atypical	X				
10		None	X				
11		Moderate			X		
12		Mild					X
13		Mild		X			
14		Nocturnal			X		
15	None	Mild					X
16		Mild	X				
17		Atypical	X				

exhibited ST segment depression of 1 mm. or greater with atrial pacing. The remaining two showed no significant ST segment depression when paced.

Eleven patients had 0 to 2 plus constricting lesions. Eight of the eleven failed to show significant ST segment depression when paced.

Comparison was made between atrial pacing and treadmill studies in 15 cases of whom 12 had coronary angiography. In 13 the stress studies agreed, and in 2 they were at variance. One of these had left ventricular hypertrophy with normal coronaries, and the other had minor but definite narrowing of a single vessel.

Five of the 12 patients who were studied by coronary angiography as well, had 3 or 4 plus constriction of at least one coronary vessel (Table 2). Four of the five had clearly positive atrial pacing and treadmill exercise studies. The response to both stress tests was negative in one case.

TABLE 2

COMPARISON OF ATRIAL PACING, TREADMILL EXERCISE, AND CORONARY ANGIOGRAPHY

Coronary Arteriography	0 To 2 plus	4 plus
Atrial Pacing	+ + - - - - -	- + + + +
Treadmill	+ - - - - - -	- + + + +

Seven of the twelve patients had coronaries with 0 to 2 plus constriction. In this group, both methods gave negative results in five cases, positive in one, and disagreed in another.

Two patients with left ventricular hypertrophy, ST segment changes at rest, and normal coronaries had positive atrial pacing tests. These cases have been eliminated from correlation of atrial pacing results with those of coronary angiography (see discussion).

Thirteen patients had typical angina pectoris. Six of this group had positive, and seven negative atrial pacing studies. Ten patients had atypical chest pain and questionable angina pectoris. Five of these were found to have positive tests (Table 3).

TABLE 3

COMPARISON OF CLINICAL DIAGNOSIS, ATRIAL PACING, AND TREADMILL STRESS STUDIES

	Atrial Pacing		Treadmill	
	positive	negative	positive	negative
Angina 13 pts.	6	7	4	3
Atypical Pain 10 pts.	5	5	2	4

Comments

The technique of atrial pacing stress electrocardiography has been used with increasing frequency in recent years as a mode of evaluating suspected coronary vascular disease.[1, 2, 4] It has also been employed safely in investigations of normal and abnormal human cardiac physiology.[5-8] We have found atrial pacing to be a safe, uncomplicated, and efficient procedure for use in our community hospital setting.

The technique is particularly useful in elderly or obese patients and those in poor physical training. One man could not increase his treadmill exercise heart rate beyond 140 because of a prosthetic leg. Several others had claudication in addition to angina pectoris as a limiting factor in exercise. Some anxious individuals have an awareness of the heartbeat or of chest muscle sensations induced by treadmill exercise which does not accompany pacemaker-induced tachycardia. An example of this was a patient whose coronary study was normal but who developed soreness in his chest apparently associated with hyperpnea on the treadmill.

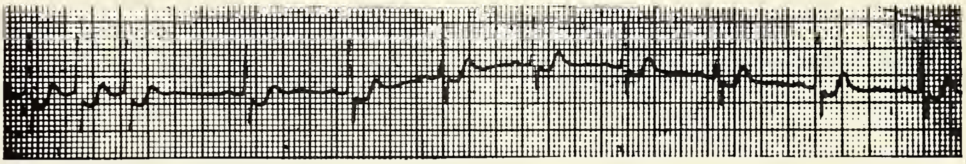
Several of our patients developed ST segment changes with atrial pacing at rates higher than those which produced similar changes during treadmill exercise. When pacing was stopped, the resting heart rate promptly recurred; and the ST segment depression reverted to normal within a few beats. With treadmill exercise, ST segment depression frequently required several minutes for complete return of both rate and ST changes to normal. Most patients who were paced developed their ST segment change during the pacing. However, treadmill patients most commonly developed ST segment changes during the recovery period—in one case, not until the eighth minute of recovery.

The prolonged ischemic change and increased heart rate of treadmill exercise is consistent with the greater oxygen debt incurred with whole body exercise. Atrial pacing has the distinct advantage of prompt cessation of ischemia when the pacing is discontinued (Fig. 1).

accuracy was slightly enhanced if both pacing and treadmill studies were done, as the two cases in which these studies disagreed had 0 to 1 plus coronary lesions.

The most important finding in our small series is the high degree of agreement between treadmill and pacing stress studies in 15 cases. This implies that, in patients unsuitable for physical exercise studies, pacing may be substituted with equal confidence in its accuracy. Though both methods missed two of six 4 plus stenotic coronary systems, evidence from a larger series of treadmill studies suggests that an accuracy of approximately 80% may be expected for both methods.[9]

Figure 1



Rapid Regression of ST Segment Depression at Cessation of Atrial Pacing.

Atrial pacing does not duplicate the hemodynamic changes of exercise. Various workers have found differing effects on cardiac output, but it is clear that the increased output of exercise is not consistently induced by pacing.[1, 5, 8] Myocardial contractility is increased by pacing but not to the degree seen with body exercise. Pacing-induced angina is associated with no change or a decrease in left ventricular end diastolic pressure in contrast to the increase seen with exercise-induced angina.[8]

In our studies we have confirmed the observation of Lau and Pitt that second degree heart block occurs commonly during atrial pacing.[2, 4] It can be readily abolished by atropine without detriment to the accuracy of the test. Its occurrence is not a reliable clue to the presence of coronary disease as defined by selective coronary arteriography. Atrioventricular block does not occur when the same patients are brought to similar heart rates by treadmill exercise. We believe that autonomic changes occur with exercise, which facilitate conduction and prevent heart block on the treadmill.

Our findings suggest that patients with left ventricular hypertrophy cannot be reliably studied by stress electrocardiography because of the occurrence of false-positive results. This may be an effect of ischemia due to increased myocardial thickness.

When the ST segment depression criterion was changed from 1 mm. to 0.5 mm., one additional 4 plus coronary stenosis was identified; but specificity was diminished by the inclusion of six false-positive results. Use of the QX/QT ratio (Lepeshkin) did not increase the value of the studies.[11] Diagnostic

Although false-negative atrial pacing studies occurred in two of six severely diseased hearts, the remaining eight negative studies represented hearts with minor lesions of grades 0 to 2 plus. Negative results were found in these eight of the total of eleven patients with 0 to 2 plus stenosed coronary systems. Thus, in our experience, a negative atrial pacing study indicates a patient unlikely to have surgically remediable coronary disease.

False-positive results of atrial pacing were more common. Three of seven positive studies represented patients with 0 to 2 plus stenoses who were not candidates for coronary surgery. It is not surprising that postive stress tests occur in the absence of severe coronary disease since adequacy of blood supply is related to tissue needs as well as to coronary patency. Ischemia and myocardial necrosis are known to occur in diverse experimental and clinical conditions in the presence of a normal coronary circulation.[10]

Atrial pacing electrocardiography offers a practical method for identifying those patients who should be further studied with selective coronary arteriography. It also helps the physician eliminate from angiographic study patients highly unlikely to have surgically remediable lesions.

Summary and Conclusions

1. Twenty-five patients with anginal chest pain were studied by atrial pacing electrocardiography. Seventeen were studied with selective coronary

angiography and the results compared. Further comparison was made in fifteen of the group who had treadmill exercise electrocardiographic studies.

2. Two thirds of the atrial-paced patients in the group with 4 plus coronary disease exhibited positive electrocardiographic findings. Three quarters of the patients with 0 to 2 plus coronary disease had negative atrial pacing studies.

3. Identification of ischemic change as level 1 mm. ST segment depression produced the most reliable correlation between visibly diseased coronary arteries and either stress test.

4. Atrial pacing has a distinct advantage over treadmill exercise in handicapped patients and is as reliable as the treadmill test.

5. Atrial pacing has a further advantage over whole-body exercise methods in the prompt remission of ischemia and exercise-induced pain when pacing is stopped.

6. Both stress tests proved valuable in selecting patients for coronary arteriography.

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Whenever a new discovery is reported to the scientific world they say first "it is probably not true."

Thereafter when the truth of the new proposition has been demonstrated beyond question they say "Yes it may be true but it is not important." Finally when sufficient time has elapsed to fully evidence its importance they say "Yes surely it is important but it is no longer new."—*Michel de Montagne*, 1533-1592, *Familiar Medical Quotations*—Maurice B. Strauss

The Pharmacology of Immunosuppressive Agents

Malcolm S. Mitchell, M.D. and Joseph R. Bertino, M.D.

Many of the chemical agents useful in the therapy of cancer have proved to be effective suppressors of the immune response in animals and in man. Such immunosuppression is useful to the host when the immunological reaction is undesirable, as in autoimmunity or in rejection of a transplanted organ, but is detrimental where the ability of the host to reject a tumor is lessened. It is clearly important whether one deals with "helpful" or "harmful" immune reactions to understand as much as possible about the drugs themselves, to achieve both maximal benefit and safety.

In this review we will briefly discuss the following aspects of this subject:

1. The classes of drugs that have immunosuppressive properties.
2. The pharmacology and mechanism of action of these drugs.
3. Differential effects upon subclasses of immunity.
4. Toxicity caused by the drugs.
5. New dosage schedules of drugs that offer the hope of a better therapeutic index.

The general classes of drug and some examples of drugs in each class are shown in Table 1.

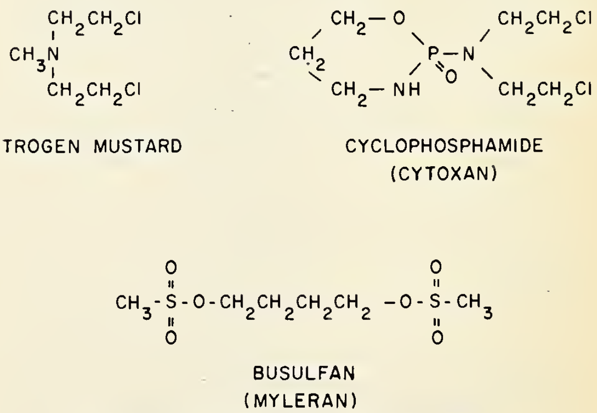
We will not discuss antilymphocyte serum although it is a potent immunosuppressive agent since an excellent account appears in Medawar's recent article.[1] Steroids, which for the most part act as lymphocytolytic or antiinflammatory agents, also will not be discussed in this account. They are very useful adjuncts, but by themselves inhibit specific immune responses only slightly.[2,3] In addition the toxicity and side effects of long-term high-dose therapy with steroids, while familiar, are nonetheless awesome, as illustrated in Table 2.[2]

Specific Agents

The alkylating agents (Fig. 1) include such drugs as nitrogen mustard (mechlorethamine, HN2*), one of the earliest cancer chemotherapeutic agents to be used in man. Although HN2 has immunosuppressive properties, two other members of the class are of particular interest, busulfan (myleran) and cyclophosphamide (Cy). Busulfan, a moderately potent agent, appears to be effective in inhibiting antibody synthesis only when given before the antigen, similar to X-rays, but differing from most other chemical agents.[5] It is a compound with a very slow onset of action, which may partially explain its unique timing. Cy is one of the most powerful immunosuppressive agents in use, inhibiting primary or secondary (memory) antibody responses.[6,7] A single large dose of Cy given one day before, concomitantly with antigen or 1-2 days afterward can produce not only immunosuppression but also immunological tolerance if the dose of antigen is high enough.[7,8] Delayed hypersensitivity reactions are strongly antagonized too.[9] Cy, a cyclic mustard, is activated by phosphamidases and phosphatases present in the plasma and in liver microsomes.[10] Con-

Figure 1

ALKYLATING AGENTS



Structure of 3 Common Alkylating Agents.

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* HN2 is a World War II chemical warfare designation and not a formula.

sequently, drugs such as phenothiazines and barbiturates that induce as increase of the microsomes may result in increased toxicity of Cy. Alkylating agents cross-link strands of DNA thus affecting intermitotic ("resting") cells and preventing replication.[11] Binding of chains of RNA and of protein also probably occurs. Other cellular synthetic and catabolic events continue, and it is this unbalanced activity that may lead to cell death. Cy also appears to have a further effect upon proliferating lymphoid cells, resembling an antimetabolite, enabling it to produce selective effects on cells specifically stimulated by antigen.[7]

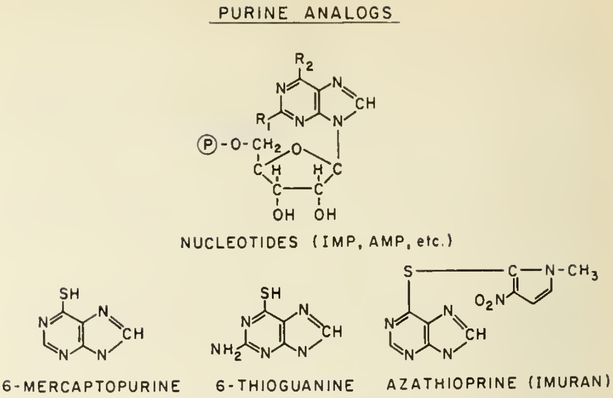
A second broad category of immunosuppressive agents is the antimetabolites, whose action depends upon inhibition of synthesis of DNA. These drugs are effective suppressants only when given after the antigen because they affect proliferating lymphoid cells. A major subdivision is the purine analogs, including 6-Mercaptopurine (6-MP, Purinethol), azathiopurine (Imuran), and thioguanine (TG, Tabloid) all of which have found extensive use in clinical situations such as organ transplantation.

TABLE 1

CLASSES OF COMMONLY USED AGENTS WITH IMMUNOSUPPRESSIVE ACTIVITY

Class of Drug	*Examples of Drugs Included in the Class*
1. Alkylating Agents	Cyclophosphamide Cytoxan, Cy) Nitrogen mustard (HN2) Chlorambucil (Leukeran) Busulfan (Myleran)
2. Antimetabolites	
a) Purine antagonists	6-Mercaptopurine (6-MP, purinethol) Azathioprine (Imuran) 6-Thioguanine (Tabloid)
b) Pyrimidine antagonists	5-Fluorouracil (5-FU), Fluorodeoxyuridine (FUDR) Bromodeoxyuridine (BUDR) Cytosine arabinoside (ara-c, cytarabine)
c) Folate analogs	Methotrexate (amethopterin, MTX)
3. Antibiotics	Antinomycins C and D, Puromycin
4. Urea derivatives	Bis-Chloroethyl-nitroso-urea (BCNU)
5. Steroids	Prednisone
6. Antibody	Antilymphocyte serum (ALS) or antilymphocyte globulin (ALG)
7. Enzymes	Asparaginase
8. Vinca Alkaloids	Vincristine (VCR), Vinblastine (VLB)
9. Methyl hydrazine derivatives	Procarbazine (Matulane)

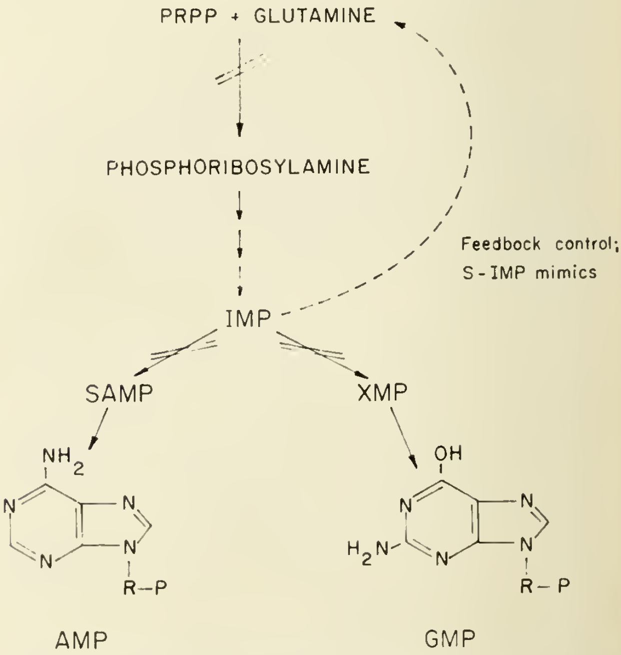
Figure 2A



Purine Analogs, Structure.

Their structure and probable mechanisms of action are shown in Fig. 2. 6-Mercaptopurine exerts several blocks in the synthesis of adenine and guanine, preventing interconversion of purine bases, especially inosinic to guanylic acid, and exerts a "pseudo-feedback" inhibition one of the earliest steps in the synthesis of purines.[12] "Pseudo-feedback" refers to an action of 6-MP after it is converted to the monophosphate form, thioinosinic acid, (S-IMP) which mimics the natural compound inosinic acid, (IMP) and by feedback prevents formation of phosphoribosylamine. In addition, a

Figure 2B



Purine Analogs, Mechanism of Action. (Redrawn After Brockman[12]). PRPP, phosphoribose pyrophosphate; IMP, inosinic acid; SAMP, adenylosuccinic acid; AMP, adenylic acid; XMP, xanthinylic acid; GMP, guanylic acid; S-IMP, thioinosinic acid.

small amount of 6-MP is incorporated into RNA and into DNA in the form of thioguanine.[13] Thioguanine itself is also incorporated into DNA approximately to the same extent.[14] The latter compound is inactivated by intestinal guanase and as a result, has little gastrointestinal toxicity, which is often limiting with 6-MP and azathiopurine.[14a] Another difference is that TG is inactivated first by deamination while 6-MP and azathiopurine are converted in the liver to thiouric acid by xanthine oxidase.[15] This means that concomitant use of the xanthine oxidase inhibitor allopurinol (Zyloprim) does not necessitate a reduction of the dose of TG as it does with the other two purine derivatives. The dose of 6-MP and azathioprine must be decreased to one-third of its usual level if allopurinol is given. Since some drug is excreted unchanged by the kidney, renal insufficiency requires lower doses too. Hitchings and Elion[16] attempted to block rapid methylation and oxidation of 6-MP by attaching an imidazolyl ring to the sulfur atom at position 6, (see Fig. 2A) creating azathioprine. However, sulfhydryl groups present *in vivo* (as on glutathione or on proteins) rapidly react with azathioprine to produce 6-MP.[15] It is still an unresolved question whether azathioprine has significant immunosuppressive activity apart from its ability to generate 6-MP. There is evidence in rodent experimental systems that azathioprine may be more potent on a molar basis and thus has independent action (Elion, personal commun.). Whatever the explanation, in man its major advantage over 6-MP presently seems to be its better therapeutic/toxic dose ratio (therapeutic index). That is, azathioprine can be used for a longer period of time than comparably effective doses of 6-MP, with less risk of leukopenia or thrombocytopenia.

TABLE 2

LATE EFFECTS ATTRIBUTED TO ADRENAL STEROIDS*

Cushingoid appearance
- Acne
- Striae
- Moon-face

Fluid retention
- Edema
- Hypokalemia

Endocrine abnormalities
- Exacerbation of diabetes
- Suppression of adrenal function
- Growth suppression in children
- Weight gain

Hematologic changes
- Ecchymoses
- Leukocytosis

Muscular
- Weakness
- Atrophy

Psychologic
- Euphoria
- Mental changes
- Insomnia

Circulatory
- Hypertension
- Cerebral-edema

Osseous
- Osteoporosis
- Pathologic and compression fraction

Gastrointestinal
- Epigastric distress
- Peptic ulcers
- Acute pancreatitis
- Ulcerative colitis?

Immunologic
- Infectious complications
  - Fungi
  - Tuberculosis

Cancer
- Increase incidence
- Acceleration of dissemination
- Metastases to unusual sites

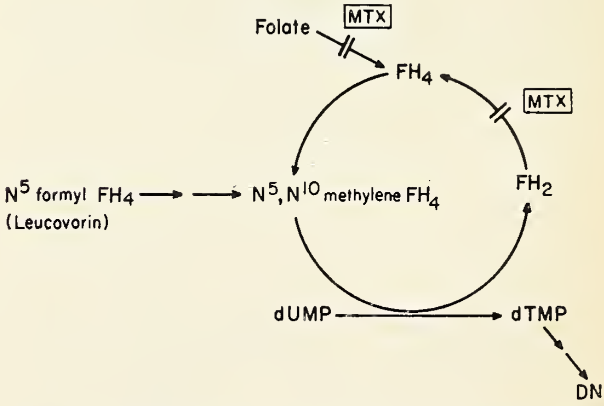
Teratogenic
- Mice, rabbits

* Reprinted with permission from Karnofsky.[4]

Among the folic acid analogs, the most important compound is methotrexate (N^{10}methyl, 4-aminopteroylglutamate, amethopterin, MTX), (Fig. 3). These antagonists bind to the enzyme dihydrofolate reductase and prevent it from catalyzing the conversion of folic acid or dihydrofolic acid to the tetrahydro form (THFA).[17] THFA is the active coenzyme form of folic acid, required in the transfer of one-carbon (formyl) groups in several biosyntheses. Most important of these is the synthesis of thymidylic acid, the pyrimidine derivative found uniquely in DNA. Thus, by inhibiting formation of THFA, MTX ultimately blocks DNA synthesis and cellular replication. MTX is not appreciably metabolized in man, although it is in some other species, and so adequate renal function is the critical factor in avoiding prolonged, severe toxicity. The vitamin citrovorum factor (N^5-formyltetrahydrofolic acid, Leucovorin) can be given after a single dose of MTX to antidote its toxic effects, ostensibly without sacrifice of therapeutic efficacy.[18, 19]

5-Fluorouracil (5-FU) or 5-fluorodeoxyuridine (FUDR), both of which must be converted *in vivo* to their nucleotide form before they are active, are pyrimidine antagonists active in immunosuppres-

Figure 3



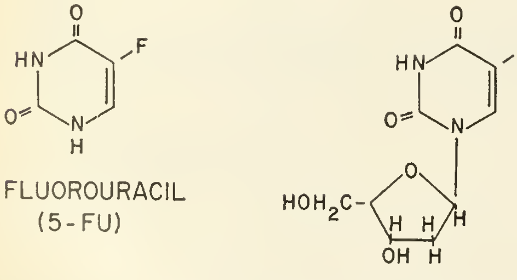
Mechanism of action of methotrexate (MTX). (Reprinted with permission from (27)). Note that MTX blocks the conversion of folate and dihydrofolate to tetrahydrofolate, both mediated by the enzyme dihydrofolate reductase. dUMP, deoxyuridine monophosphate; dTMP, thymidine monophosphate, FH$_2$, dihydrofolic acid; FH$_4$, tetrahydrofolic acid.

sion (Fig. 4). In several experimental animal models neither drug is active as an immunosuppressant but in man unequivocal evidence has been obtained of such effects on both antibody synthesis and the induction of delayed hypersensitivity.[20, 21] Bromodeoxyuridine (BUDR), but curiously *not* the seemingly closely related iododeoxyuridine (IUDR) also is immunosuppressive, in rabbits. 5-FU or FUDR act to inhibit the same step as does MTX, conversion of deoxyuridylate to thymidylate, but by competitive inhibitory binding of the enzyme thymidylic synthetase.[22] Effects on RNA are probably not a major mode of action of 5-FU in man, nor is there significant incorporation of 5-FU into DNA. 5-FU is detoxified by the liver and should be used cautiously in the presence of severe hepatic dysfunction.

A new departure in pyrimidine analogs is cytosine arabinoside (cytarabine, ara-C) whose sugar moiety is altered rather than its base (Fig. 5). The compound inhibits conversion of deoxyuridine diphosphate to deoxycytidine diphosphate during the synthesis of DNA,[23] inhibits polymerization of triphosphates into DNA[24] and is itself incorporated into fraudulent DNA and RNA to some extent.[25] All of these actions depend on prior phosphorylation of ara-C, which is subsequently rapidly inactivated by deamination in the liver to uracil arabinoside. Despite rapid inactivation, daily single doses are effective as immunosuppressants in rodents and in man,[26, 27] although short-term high-dose infusions appear to be more potent.[27]

Other drugs used in chemotherapy of cancer have immunosuppressive properties, including actinomycins C and D, and the vinca alkaloids vincristine (Oncovin, VCR) and vinblastine (Velban). Actinomycins C and D have been used as adjunctive measures in renal transplantation but have profound toxicity to normal epithelium and bone marrow cells. Their mechanism of action is blockage of DNA-dependent RNA synthesis, by binding to the template DNA.[28] There is no attachment to RNA. The vinca alkaloids principally inhibit formation of intracellular microtubules, the structures that form the mitotic spindle.[29] They thereby inhibit cell division but additionally they can decrease DNA and RNA synthesis and the formation of phospholipids.[30]

Figure 4



5-FLUOROURACIL
(5-FU)

5-FLUORODEOXYURIDINE
(5-FUdR)

5-Fluorouracil and 5-Fluro-2-deoxyuridine, pyrimidine antagnoists.

Differential Effects on Immunity

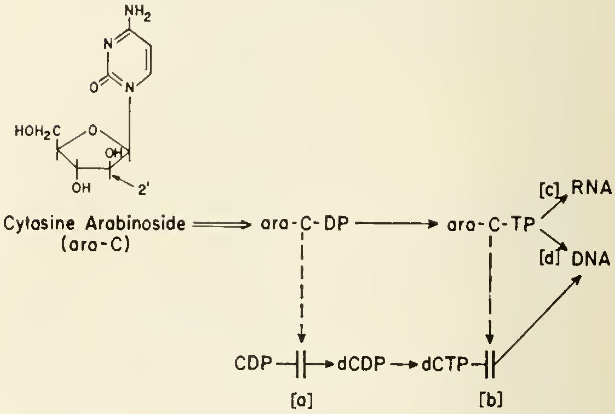
There are a number of excellent reviews discussing the detailed effects of these drugs upon immune reactions.[31-33] In brief, they are all capable of suppressing the following reactions, listed in the usual order of susceptibility to increasing doses:

A) Delayed hypersensitivity reactions, such as the induction of skin sensitivity to dinitrochlorobenzene.

B) 1. Serum IgG (γG) antibody in the primary immune response to a specific antigen, such as sheep red blood cells or *E. coli* Vi (capsular) antigen.
   2. Serum IgM (γM) antibody in the primary immune response.

C) Serum antibody (usually IgG) in a secondary (anamnestic) response to an antigen such as tetanus toxoid.

Figure 5



Structure and mechanisms of action of cytosine arabinoside (Ara-C). (Reprinted with permission from (27)). Ara-C differs from the cytosine at the 2′ and 3′ positions of the sugar moiety, where the hydrogens are in the trans rather than cis configuration. Inhibition of the conversion of cytidine diphosphate a, and of deoxyribonucleic acid (DNA) polymerase b have been demonstrated. The known incorporation of ara-C into both DNA and ribonucleic acid (RNA) may also be significant elements in its rapid activity. Ara-C-DP and ara-C-TP, di- and tri-phosphate derivatives of ara-C; CDP, cytidine diphosphate; dCDP and dCTP, di- and tri-phosphate forms of deoxycytidine.

Established delayed hypersensitivity and pre-existent antibody titers usually are unaffected.

Certain dosage schedules (i.e., timing or dosage level) can selectively inhibit only one of these components, and a few can actually augment the selected responses.[34] MTX may be an exception in that antibody synthesis seems more sensitive to its action than is delayed hypersensitivity.[35] Selective induction of immunological tolerance (specific inability to respond) to an antigen can be accomplished in adult animals by administering large doses of antigen with the alkylating agent Cy,[7, 8] with procarbazine (Matulane)[36] or with the antimetabolites, ara-C,[8] 5-FU[20] or 6-MP.[32] Thus the drugs can have more subtle effects than their "blockbuster" actions upon nucleic acid synthesis and replication might seem to imply, if they are manipulated properly. It should be emphasized however that the clinical usefulness of all of these agents may not depend upon their specific immunological effects but upon anti-inflammatory properties or other processes unknown to us. Definitive proof of an immunosuppressive mechanism in a given disease depends upon measurement of changes induced by the drug in the specific immunological abnormality associated with the disease, but that has only rarely been possible.

Toxicity

Cancer chemotherapists are often willing to accept some toxicity in dealing with these powerful agents, but patients with immunological disorders often have a more benign chronic illness. "Brink of disaster" therapy is inappropriate in many forms of cancer and certainly is even less appropriate in immunosuppressive therapy. For this reason, it is important for the clinician to be aware of known toxicity, side effects and potential hazards before embarking upon any immunosuppressive therapy.

1. Toxicity of Short-term Treatment

All cytotoxic agents act on rapidly growing cells, both normal and abnormal. These cells include not only antigen-stimulated lymphocytes or cancer cells but also gastrointestinal, epithelial and bone marrow stem cells. Therefore, except for prednisone, all of the agents we have mentioned depress formation of bone marrow cells and may lead to some degree of reticulocytopenia, leukopenia and thrombocytopenia. Cyclophosphamide and vinblastine cause granulocytopenia but seem to cause relatively less thrombocytopenia, a "platelet sparing" effect. Vincristine at all but large doses spares all bone marrow elements, causing primarily neurological toxicity (paresthesias, loss of deep tendon reflexes, etc.). Effects upon gastrointestinal epithelium, as reflected by variable degrees of nausea, vomiting and stomatitis (mucositis), are common to most of the drugs discussed even after parenteral administration. Actinomycin D, 5-FU and MTX are particularly liable to cause diffuse gastrointestinal irritation and ulceration. Diarrhea or frank lower gastrointestinal bleeding may ensue, requiring several days to resolve.

Hemorrhagic cystitis due to cytotoxic metabolites of Cy occurs with high doses of drug, but is preventable to some extent by large intake of fluids.

Alopecia, caused by inhibition of rapidly proliferating epithelial cells in the hair follicle, is a theoretical toxic effect of all these drugs, but is particularly common with high doses of Cy, Actinomycin D, and VCR. It has been claimed recently that placement of a tourniquet around the forehead during and shortly after the period of administration of rapidly cleared agents such as cytoxan can prevent alopecia.[37] Regrowth of hair frequently occurs even while therapy is continued in any event. A similar but cosmetically less significant disorder of epithelial cells is arrest of growth of the nail, seen with actinomycin D or alkylating agent therapy.

2. Risks of Long-Term Therapy (Table 3)

Long-lived aplasia of the bone marrow is exceedingly uncommon with antimetabolites but has occurred after the intensive use of alkylating agents such as thio-TEPA and busulfan. Any alkylating agent used in high dosages or for a long period of time has the potential to destroy stem cells and should be used with suitable caution.

Hepatic fibrosis has been noted in children with acute leukemia who received 6-MP or MTX chronically.[38] These children were chronically ill and had received many other drugs, but the relationship to these two antimetabolites appeared to be real. Busulfan has caused pulmonary fibrosis following long-term administration, as well as diffuse hyperpigmentation. The latter is seen also during chronic administration of actinomycin D, for uncertain reasons.

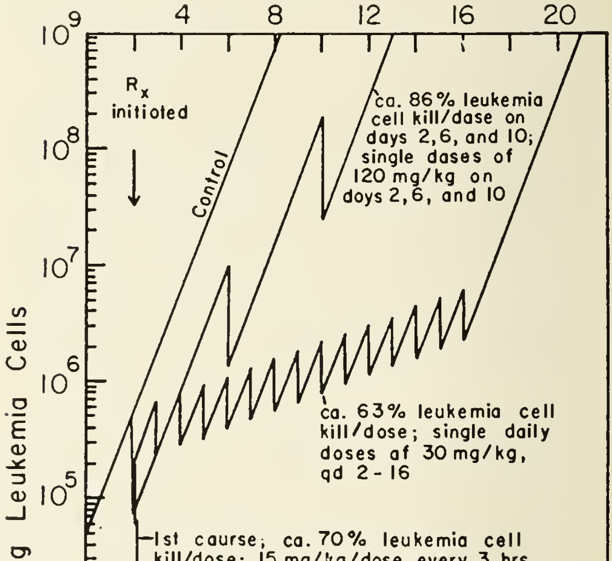
A theoretical hazard is alteration of the germplasm in long-term recipients of these agents. No firm evidence exists that this has occurred in man. In fact several normal pregnancies have been reported in women receiving azathioprine after a renal transplant.[39, 40] It is still a difficult theoretical objection to counter, however, and should certainly be kept in mind as a possibility. Certainly several of the antimetabolites have documented potency as abortifacients, and by analogy with cytotoxic physical agents (e.g., X-rays) cytotoxic drugs may possibly cause chromosomal breaks. Administration of *any* drug during pregnancy of course should be done only if absolutely necessary, to avoid teratogenic or toxic effects upon the fetus.

A further menacing possibility, backed by experimental work and by data in man, is the production of diminished resistance to or actual induction of cancer by cytotoxic agents. Procarbazine, a methylhydrazine derivative used in Hodgkin's disease (shown to be highly immunosuppressive in mice) and chlornaphazine, an alkylating agent whose use had been abandoned, are potent carcinogens in animals.[41] It has been demonstrated in mice that the experimental hydrocarbon carcinogens such as methylcholanthrene are potent immunosuppressive agents, and that there is a strong correlation between their immunosuppressive activity and ability to induce cancer.[42, 43] Anti-lymphocyte serum, X-rays and other measures designed to decrease host immunity have made viral leukemias easier to induce in mice. In man, at least 5 patients who received renal transplants have since developed lymphomas,[44] and a renal neoplasm accidentally transferred was not rejected by the recipient until immunosuppressive therapy was stopped.[45] The latter finding suggests that a basic surveillance mechanism for cancer broke down, rather than that lymphoid tissue was somehow made to grow abnormally by immunosuppressive drugs. If in fact our immunological defenses are basically designed, as Sir F. M. Burnet suggests, to ward off spontaneously arising tumor cells, prolonged immunosuppression obviously must be justified by the severity of the aberrant process requiring treatment.

New Dosage Schedules

Improvement of dosage schedules of the immunosuppressive drugs to achieve a better therapeutic index has been of considerable interest to us, and extends logically from studies in neoplastic disease. It is clear that cells having a short generation time, one obtains greater cell kill and less injury to normal marrow if high intermittent doses are used. Figure 6 shows the effect of cytosine arabinoside upon L1210 leukemia when the drug is given as 1) a single subcutaneous dose every fourth day, 2) daily doses for 15 days or 3) in divided doses over a 24 hour period every four days.[46] The single doses every fourth day kill only a small percent of the tumor cells and the animals die in 13 days. Better cytotoxicity is achieved with the daily doses but cures (i.e. complete eradication of tumor cells) are achieved only with the high dose intermittent therapy. Antigen-stimulated lymphoid cells have generation times on the order of 7-14 hours, shorter than bone marrow stem cells, and theoretically should be more profoundly affected by the intermittent doses of antimetabolites than by the daily doses now routinely employed. It should be emphasized that these intermittent dosage schedules are less toxic than or at most equally toxic as daily schedules, so that there is a true therapeutic gain. We have some data in man to indicate the effect of such regimens, but their utility after transplantation has not yet been established. Furthermore, it is clear from many studies that one need not carry any of these drugs to toxicity to achieve optimal im-

Figure 6

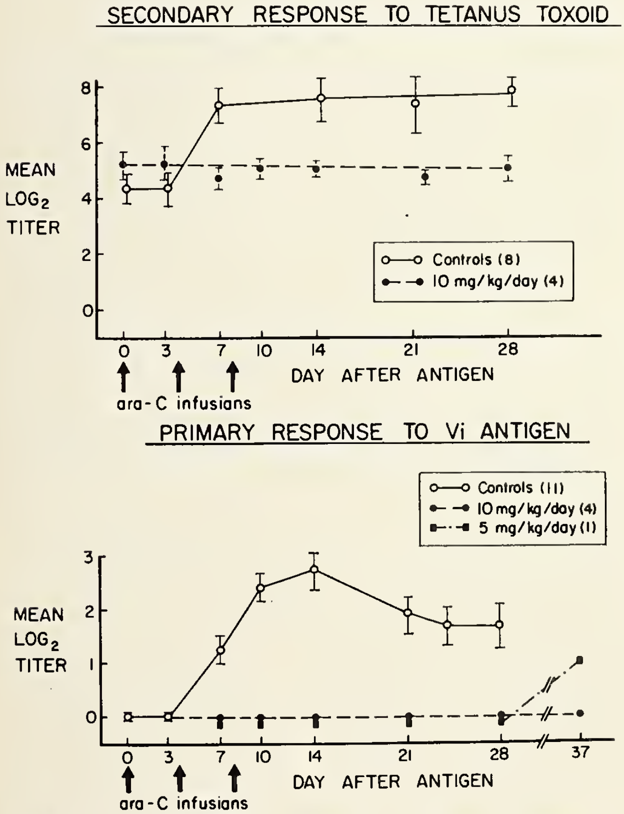


Effect of different dosage schedules of cytosine arabinoside upon murine L-1210 leukemia. (Reprinted with permission from (46)).

munosuppression. The degree of leukopenia should not be the index of efficacy but only a limit to the dose that can be administered.

Figure 7 shows that 10 mg/kg infusions of ara-c abolished the primary and secondary responses to antigens in patients with solid tumors. Figure 8 extends these observations to MTX infusions, which also demonstrate one other approach to less toxic immunosuppression: that of giving the antidote after the drug. Berenbaum and Brown[18] have shown that Citrovorum factor given after MTX permits suppression of rodent allograft rejection with lower toxicity than the same dose of MTX alone. In our studies,[27] as many as 11 consecutive infusions of MTX + Citrovorum factor were given at 4 day intervals. Approximately 60% of the patients had complete immunosuppression; the remainder produced only an IgM response. Those patients producing antibody did so within 2 weeks of discontinuing the infusions regardless of the number of infusions, indicating rapid recovering of their immunological mechanisms. Leukopenia and thrombocytopenia were minor despite the high doses of drug employed, probably attributable both to the scheduling and to the sequential use of the antidote.

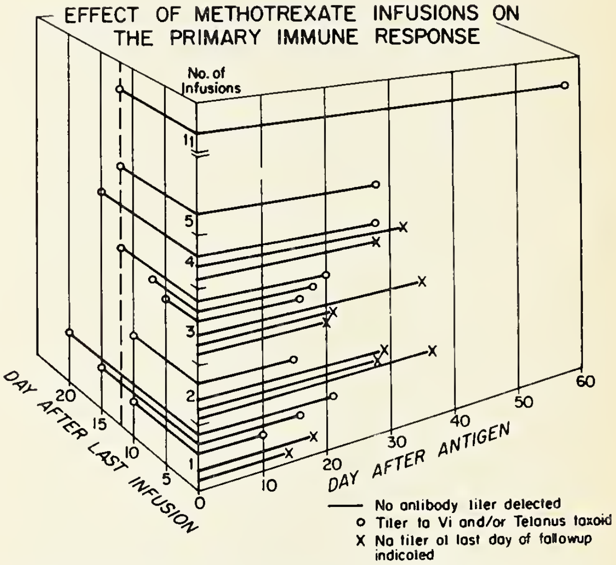
Figure 7



Effects of intermittent infusions of cytosine arabinoside upon antibody formation in man. (Reprinted with permission from (27)).

In conclusion, it seems fair to say that immunosuppressive agents are potent chemicals with capacity to injure or destroy a variety of host cells, but that they can be used to produce beneficial effects in serious diseases by judicious handling. Just as chemotherapists are beginning to understand the use of these drugs in cancer therapy, so a knowledge of optimal therapeutic regimens in immunological disorders is now being gained by analogy and by testing in direct experiments.

Figure 8



Effects of infusions of methotrexate followed by citrovorum factor upon the primary immune response in man. (Reprinted with permission from (27)).

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Splenectomy as an Adjunct to the Treatment of Hodgkin's Disease

Sherwin B. Nuland, M.D.

Present methods of treating Hodgkin's disease depend for their success upon accurate assessment of the extent of involvement.[4] Any error in determining the distribution of disease in a given patient may lead to a plan of treatment which in the long run will prove futile. Particularly now that curative therapy is a real possibility, the spectre of undertreating any patient looms as a potential tragedy, should areas of involvement be missed. At the same time, it has become particularly important to discover which of the apparent candidates for radical radio-therapy are already beyond the curative stage, so that these patients can benefit from the great strides being made in the field of chemotherapy.

Utilizing careful and repeated clinical examination, multiple types of blood studies, liver and bone marrow biopsies, organ scanning techniques, and, most recently, the rapidly improving methods of lymphangiography, it has been possible to reach a reasonably good estimate of the staging of disease in most patients. However, it is clear that all of these methods, and even their sum total, have limitations, whether these be in the techniques themselves, in their interpretation or in the relevance of the information derived to the state of involvement.

It has become apparent from a study of my own patients, as well as the work of others, that direct biopsy of tissue is the most accurate method of determining extent of disease.[1, 2] In evaluating Hodgkin's disease in the abdomen this requires laparotomy. If, in addition to helping obtain accurate diagnosis, a laparotomy can afford any facilitation of subsequent therapy, such an operation becomes a justifiable undertaking, provided that it can be done without significant morbidity. To show that the three criteria of evaluation, facilitation and safety can be met by the procedure of abdominal exploration and splenectomy is the purpose of this presentation.

Methods

Prior to operation each patient is evaluated by the clinical methods indicated above. Following review of the data thus obtained, a tentative staging is made of his disease process. The classification used has been that proposed by the conference on Hodgkin's disease at Rye, New York in September, 1965 (Table 1).[6] At this point a decision is reached as to the optimal method of management.

Patients with stage I A and B, II A and B and III A disease are treated with curative radical radiation therapy. Most stage III B and all stage IV patients are primarily candidates for chemotherapy. Under certain limited conditions, patients with III B disease receive radiation as their primary treatment. These conditions are described elsewhere in this series of reports, and are designed to select the approximately 15% of III B patients who have been reported to be curable with such treatment.

The only patients who are not operated upon are those who are too ill to withstand surgery, either because of the Hodgkin's disease or an intercurrent medical condition. In stage I A, II A and III A patients laparotomy is carried out following radiation therapy to the mantle portal. This timing is used to take advantage of the splenectomy effect of temporarily raised peripheral blood counts, which

TABLE 1

STAGING OF LYMPHOMAS

Stage I.	Disease limited to 1 anatomic region or to 2 contiguous anatomic regions on the same side of the diaphragm
Stage II.	Disease in more than 2 anatomic regions or in 2 noncontiguous anatomic regions on the same side of the diaphragm
Stage III.	Disease on both sides of the diaphragm but not extending beyond the involvement of lymph nodes, spleen and/or Waldeyer's ring
Stage IV.	Involvement of the bone marrow, lung parenchyma, pleura, liver, bone, skin, kidneys, gastrointestinal tract or any tissue or organ in addition to lymph nodes, spleen or Waldeyer's ring

A and B subclasses indicate absence or presence of systemic symptoms respectively. The following documented symtoms are significant: (a) fever; (b) night sweats: (c) pruritus.

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facilitates hemotological tolerance to any subsequent abdominal irradiation. Patients who are stages III B and IV undergo laparotomy prior to the commencement of chemotherapy, as do those who are thought to be I B and II B, in view of the probability that these latter will prove at exploration, to be more advanced.

All operations have been carried out through a left rectus-splitting incision from the costal margin to a point a few centimeters superior to the umbilicus. With minimal retraction this gives excellent exposure for visualizing not only the length of the aorta, but of the common iliac arteries as well. Careful palpation of all organs is now carried out, with particular attention being paid to the usual sites of nodal tissue. Any nodes which either feel suspicious or which, on the lymphangiogram, look possibly diseased are now removed through short, separate incisions in the posterior peritoneum. If there are no suspicious node areas, sample nodes are removed from both sides of the aorta, at the approximate L2 position. Hemostasis is achieved by metallic clips, which have the added advantage of clearly pointing out the positions of these nodes on postoperative films.

Following the node biopsies, a generous opening is made in the gastrocolic omentum and palpation of the entire length of the splenic artery is carried out. This sometimes reveals suspicious nodes at the celiac axis, which can be biopsied and clipped. At this point, the proximal splenic artery is dissected out of the superior surface of the pancreas, about two to three inches lateral to the celiac axis, and ligated. Clips are placed at the point of ligation. Splenectomy is begun in the usual fashion by dividing the spleno-renal ligament posteriorly and the vasa brevia anteriorly, and bringing the spleen up into the wound. Depending somewhat on the anatomical relationship of the splenic pedicle to the tail of the pancreas, it has usually been possible to carry the dissection of the splenic artery and vein a few inches medialward along the superior surface of the pancreatic tail. This serves the double purpose of picking up and removing splenic pedicle lymph nodes which might otherwise have been missed, and at the same time allows the subsequent radiation field to avoid the left kidney. Metallic clips are now placed into the divided stump of the splenic artery. The clips at the proximal and distal portion of the artery outline its position and extent. Both wedge and needle biopsy of the left lobe of the liver are now taken, and the abdomen is closed. A nasogastric tube that was inserted prior to the induction of anesthesia is removed as soon as the patient awakens in the recovery room. Some patients have had appendectomy performed prior to closure.

In almost every case the radiotherapist or chemotherapist most closely involved with the patient has been present in the room throughout the operative procedure. This has allowed him not only to see the gross extent of the disease and the areas biopsied, but to make any suggestions for further biopsies that may seem indicated.

Results

This procedure has thus far been carried out by the author for twenty patients with Hodgkin's disease. There has been no significant complication. Three patients had a transient period of minor atelectatic change at the left pulmonary base associated with a slightly elevated diaphragm. In two of these individuals the spleen was at least three times normal size, and the third patient was a 63 year old man with a long history of heavy smoking. In no case did these findings persist. No blood transfusions have been necessary, except in the case of two patients who were markedly anemic on admission, and who needed blood in preparation for operation. The average postoperative hospitalization has been seven days, with the longest stay being ten days. All patients have either begun or resumed therapy within a week of discharge.

TABLE 2

	Stage						
Name	*Pre-op*	*Post-op*	*Lymphangiogram*	*Aortic nodes*	*Splenic nodes*	*Spleen*	*Spleen Weight*
							gms
J. B.	III A	III A	+	+	+	—	195
S. L.	III A	III A	+	+	+	+	180
R. S.	I A	I A	—	—	—	—	120
D. T.	II A	III A	—	+	+	+	900
P. F.	II A	II A	—	—	—	—	190
N. H.	III A	III A	+	+	not reported	—	76
K. M.	III A	III A	+	+	+	+	110
A. H.	II A	III A	—	+	+	+	185
Y. D.	I A	III A	Equiv.	—	+	—	288
J. M.	I A	I A	—	—	—	—	163
A. B.	III A	II A	+	—	—	—	153
G. W.	I A	I A	Equiv.	—	—	—	110
D. N.	I A	I A	—	—	—	—	260
D. P.	I A	III A	—	+	+	+	150
C. L.	III B	III B	+	+	+	+	500
J. G.	I B	I B	—	—	—	—	450
W. D.	III A	III A	+	+	+	+	150
D. C.	II B	II B	Equiv.	—	—	—	250
W. M.	I A	I A	—	—	—	—	500
E. D.	I A	III A	—	+	+	+	110

+ = Histologically Positive for Lymphoma
— = Negative

The results of the diagnostic aspects of this procedure are summarized in Table 2.

It is clear that in a significant proportion of patients, laparotomy indicated an extent of disease that could not have been shown by any other means. All patients in whom either spleen or splenic hilar nodes were positive fell into this category. There are ten such in the group of twenty. There are six patients in whom the classification of disease had to be changed from its preoperative estimate, five to a more and one to a less advanced stage. In five instances lymphangiogram interpretations were in error. Perusal of Table 2 shows that in eleven patients information was obtained by the surgical procedure which was either different from or in addition to what all preoperative evaluations could have predicted.

Discussion

Three criteria have been established at this institution which must be met in order to justify exploratory surgery for patients with Hodgkin's disease. That the criteria of safety and evaluation of pathology have been satisfied is clear from the above data. Based on this experience it has become increasingly evident that judgments of extent of disease are hazardous without the tissue evidence provided by laparotomy. In our experience and that of others, a high proportion of patients will harbor disease that is either unsuspected or unprovable without laparotomy, and a certain smaller group may be found to have less extensive involvement than preoperative evaluation indicates.[1, 2]

That the particular surgical technique is of paramount importance is indicated by the two patients whose spleens were negative, but whose splenic hilar nodes were positive. Had not a dissection of the artery been done back along the pancreatic tail, these nodes would not have been removed with the specimen.

The third criterion mentioned is facilitation of treatment. With the spleen removed, as well as a few inches of the distal splenic artery and vein, there is no need to irradiate the peripheral portion of the left upper quadrant. By clipping the splenic artery proximally and at its divided stump, accurate irradiation along that vessel allows shielding of the upper pole of the kidney, the lower lobe of the left lung and the stomach. Not only are these organs thereby spared, but the total irradiation time is shortened by about 4 weeks because of the reduction in field size.

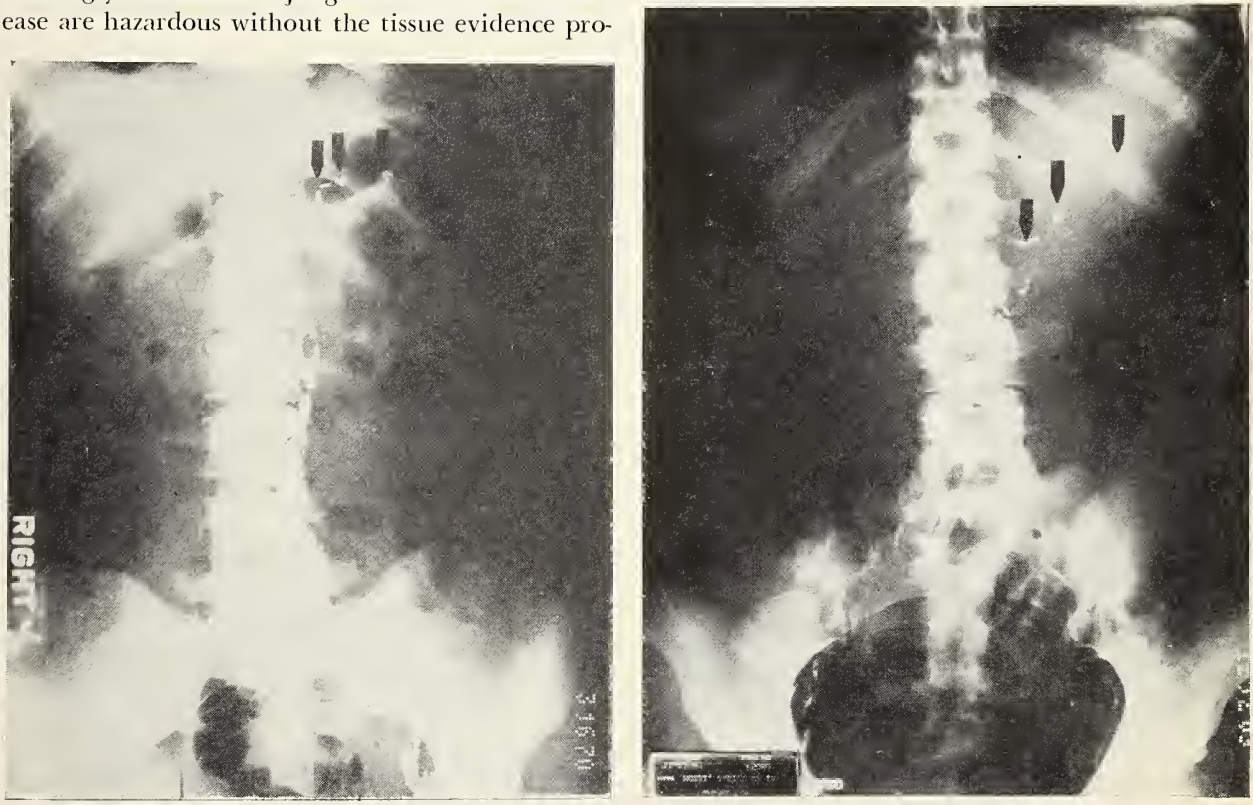

Figure 1A

Figure 1B

Appearance of post-operative X-ray. The three arrows point to a sequqence of double clips placed on the splenic artery. The positions of the clips are, respectively: the celiac axis, the proximal portion of the artery in the lesser sac, and the ligated stump at the splenic hilum. Other clips can be seen at sites of removal of peri-aortic nodes.

Splenectomy may, in addition, improve tolerance to both chemotherapy and radiation therapy. Anemia, thrombocytopenia and leukopenia seldom are problems in the operated patients. The benefit to hypersplenic patients is readily apparent.[3]

In addition to the benefits gained by specific patients a standardized treatment program creates the opportunity to increase our general understanding of a disease process. Some of these gains must be considered here. For example, the opportunity to have a tissue biopsy of nodes demonstrated by lymphangiography adds to our ability to accurately interpret this diagnostic procedure. Also, correlating liver function tests with surgically obtained material will prove of considerable value. For example, our series has not produced a single positive liver biopsy, an outcome different from those reported elsewhere.[2] At the same time, however, only one of our twenty patients had abnormal liver function studies, which may prove, over a series of several hundred cases to have some significance. As more operated patients are followed for long periods of time, some to the autopsy tables, the roles of inadequate sampling and differences in pathological criteria can be evaluated.

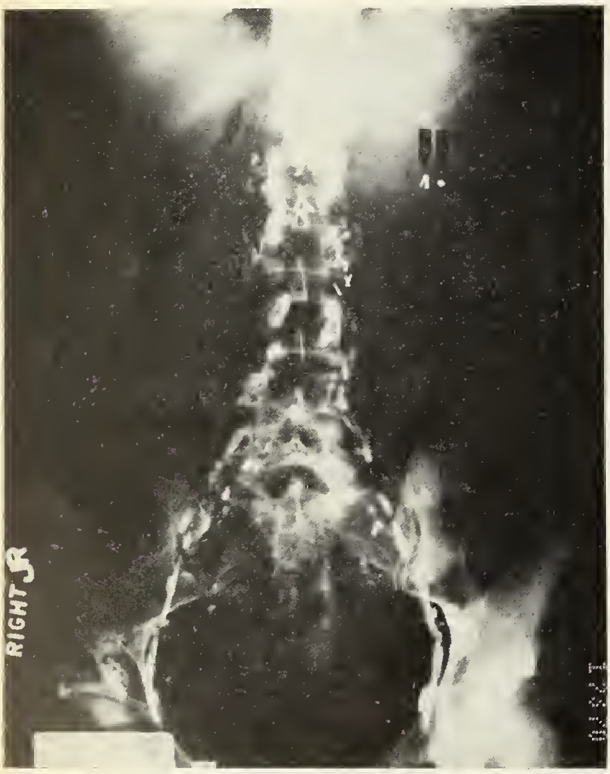

Figure 2

Illustrating how far medially the splenic vessels can often be dissected. The two arrows point to the sites of double clipping: in the lesser sac, and at the ligated splenic artery stump. In this patient, no clips have been placed at the celiac axis.

The concept of a predictably sequential and contiguous mode of spread of Hodgkin's disease from its original focus lies at the basis of therapy.[5] Examination of histological changes in nodal tissue removed from various abdominal areas may shed further light on the applicability of that concept. In this regard, the present series includes the two above-mentioned patients whose splenic hilar nodes were positive but whose spleens contained no foci of disease, while all patients with positive spleens had positive nodes at the hilum as well. There is one additional patient in whom the histological changes in the hilar nodes were more advanced and easily recognized than those in the spleen. These findings add support to the concept of contiguity of spread, and increase our confidence in the rationale of therapy.

Any discussion of the surgeon's role in Hodgkin's disease would be incomplete without some mention of the operation that has come to be known as oophoropexy. Irradiation of the pelvis in young women with the ovaries in normal position leads to ablation of ovarian function in all instances. Following the lead of the Stanford group,[7] we have, utilizing a small suprapubic incision, moved the ovaries of young women who are about to undergo a course of such therapy. The ovaries are marked with metallic clips and sutured in the midline, one to the front and one to the back of the lowermost portion of the uterus, away from the pelvic nodes. This can be easily done, usually without cutting any ligamentous attachments, and in such a way that each tube describes a gentle curve. The radiotherapist can then shield the ovaries from the subsequent treatment field. Thusfar, although the results are encouraging, our series is too small and the follow-up too short to make any judgements about the value of this procedure.

Summary

A technique is described by which twenty patients have undergone splenectomy and multiple biopsies in the evaluation of Hodgkin's disease.

This operation can be done without complications and provides information that cannot otherwise be obtained. Such information is vital in planning appropriate therapy for each patient.

In addition, removing the spleen and its pedicle facilitates the treatment, whether by irradiation or chemotherapy or both.

In selected cases, repositioning the ovaries may protect their function.

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The Management of Hodgkin's Disease: Evolution of Radiotherapy Concepts

Raul Vera, M.D., Leonard R. Prosnitz, M.D.,
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I. Introduction

Until approximately five to ten years ago, Hodgkin's disease was generally considered to be incurable, and one still finds references in popular textbooks so stating. However, since that time a series of developments has gradually convinced physicians working in this rather specialized field that a very high percentage of all patients with Hodgkin's disease can be cured by appropriate radiation therapy. The first individuals to write in terms of actual cure rather than simply long-term remissions were Easson and Russell when they reported their results in 1963.[1] Easson and Russell considered that a group of patients was cured of Hodgkin's disease when their chances of dying from any cause including Hodgkin's disease became the same as that of the normal population matched for age and sex. Using this definition, they were able to show that after a certain number of years, usually between three and five, the survival curve of patients with Hodgkin's disease who had been treated and were free of disease became parallel to that of the general population. This indicated that Hodgkin's disease can be cured in a high proportion of patients, quite aside from the occasional long-term remission seen in patients given no treatment or only minimal palliative treatment.

When adjusting to this new optimism, it is helpful to recognize some of the reasons for the failure to cure Hodgkin's disease in past years. One reason is that the dose of radiation therapy applied to regions with known disease was often too low to even control the disease locally, as demonstrated by Kaplan's review of published local recurrence rates versus dose of radiation used.[2] These data indicate that local doses of less than 3000 rads delivered in approximately three weeks time will not reliably control local disease. It is interesting to point out that frequently low doses were delivered on the presumption that the disease was incurable, whereas it appears the low doses were the reason why the disease was not cured.

The second major reason for failure was that all areas involved with Hodgkin's disease were not treated. As will be indicated subsequently, Hodgkin's disease is often much more extensive than previously thought or easily identified by simple physical examination. Though it may begin in a local focus, either a single node or group of adjacent lymph nodes, it soon spreads to other lymph node bearing areas and eventually throughout the patient. Prophylactic irradiation of adjacent lymph node areas ostensibly free of disease appears to prevent dissemination of the disease. This is the rationale behind the use of extended fields of radiation to be described below. In summary, current management of this disease in all but late stages demands radiotherapy to the major lymph node bearing areas of the neck and trunk to relatively high doses. This is well tolerated by the patient.

II. Staging and Clinical Evaluation

It is essential to determine as accurately as possible the full extent of involvement in any patient with Hodgkin's disease in order to plan the treatment. Depending on the areas involved, the patient may fall into one of four stages, which are described in Table 1. The presence or absence of systemic symptoms is quite important both in the prognosis and determining subsequent treatment. The symptoms should be persistent in order to be considered significant. Frequently, patients will have transient fevers secondary to an upper respiratory infection or a diagnostic procedure, such as a

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lymphangiogram. Such transient symptoms are not of significance. General symptoms and signs such as malaise, anorexia, weight loss and anemia, while important, are not officially considered for staging purposes. Similarly, local symptoms such as cough due to a mediastinal mass are not considered significant for staging purposes.

In order to stage a patient accurately the following procedures should be carried out:

1. Complete history and careful physical examination with special attention paid to all lymph node bearing areas.
2. Chest X-ray and laminograms.
3. Lymphangiogram, intravenous pyelogram (IVP) and inferior vena cavagram (IVC). The latter is done in doubtful cases in order to visualize better the upper para-aortic nodes. The IVP is done at the same time as the lymphangiogram to define better the size of the visualized nodes.
4. Blood studies including complete blood count (CBC), liver function studies, blood urea nitrogen (BUN).
5. Liver and spleen scan.
6. Bone marrow aspirate and biopsy since Hodgkin's disease is rarely detected on the aspirate alone.
7. Laparotomy. This will be discussed later in detail.

III. Lymphangiography, Laparotomy and Splenectomy

In the early 1960's lymphagiography was developed as a technique for visualizing abdominal lymph nodes which could usually not be felt on physical examination nor detected by more conventional X-ray studies such as intravenous pyelogram. It soon became apparent that abdominal disease was present in a number of patients who had been thought to have disease only above the diaphragm on clinical grounds. Precisely what number of patients have disease in the abdomen detected by lymphangiography is a matter of some debate with estimates ranging from 6 to 40 per cent.[3, 4] The reason for the dispute probably is that in a number of instances, lymphangiography does not give a clear-cut answer as to the status of the abdominal nodes. The diagnostic radiologists may interpret the nodes as "suspicious" or "equivocal," neither clearly negative or positive.

TABLE 1

STAGING OF LYMPHOMAS

Stage I.	Disease limited to 1 anatomic region or to 2 contiguous anatomic regions on the same side of the diaphragm.
Stage II.	Disease in more than 2 anatomic regions or in 2 non-contiguous anatomic regions on the same side of the diaphragm.
Stage III.	Disease on both sides of the diaphragm but not extending beyond the involvement of lymph nodes, spleen and/or Waldeyer's ring.
Stage IV.	Involvement of the bone marrow, lung parenchyma, pleura, liver, bone, skin, kidneys, gastrointestinal tract or any tissue or organ in addition to lymph nodes, spleen or Waldeyer's ring.

A and B subclasses indicate absence or presence of systemic symptoms respectively. The following documented symptoms are significant: (a) fever; (b) night sweats; (c) pruritis.

We were thus led to performing exploratory laparotomy for diagnostic purposes in some patients with equivocal lymphangiograms. The spleen was also removed both for diagnosis and to simplify subsequent radiation therapy. The finding of unsuspected disease in the abdomen in the first few patients operated on have led us to extend this procedure to virtually all patients seen in our institution. The chief exceptions are those patients in whom a medical contraindication to surgery exists.

The operation is both diagnostic and facilitates subsequent therapy. Tissue is obtained from the para-aortic nodes, splenic hilar nodes, liver, any suspicious mesenteric nodes, and, of course, the entire spleen itself is available for histologic examination. Splenic hilar nodes in particular have proved to be a site of disease even when nothing else in the abdomen was involved. These nodes are not filled on lymphangiography.

Briefly the operation consists of 1) Biopsing any para-aortic nodes that appear suspicious on the lymphangiogram or any that feel suspicious on exploration. If there are none that are suspicious random node biopsy is done. 2) Any suspicious mesenteric, porta-hepatis nodes, celiac axis nodes, etc. are biopsied. 3) Wedge and needle biopsy of the left lobe of the liver is done. 4) The spleen is removed and splenic pedicle dissected back toward the aorta. The details are described by Dr. Nuland in the accompanying article.

Thus far, 33 patients have undergone exploration. Of these, 22 were stage I or II with disease limited to above the diaphragm on clinical examination and laboratory testing including lymphangiography. Six of the 22 were found to have disease within the abdomen. *This disease would have been overlooked by conventional staging methods.* Equivocal lymphangiograms were obtained in 8 patients, 3 of whom turned out to have abdominal disease at laparotomy. Thus 5 patients were spared possible unnecessary radiation therapy. These 8 patients were all staged either stage I or II in accordance with the general priciple of understaging when in doubt. Similar results have been reported by Glatstein et al.[5]

The value of laparotomy and splenectomy from a diagnostic standpoint seems clear from the above. Removal of the spleen also has the advantage of making subsequent radiotherapy easier. If the spleen were left *in situ* it would have to be irradiated. This would involve treating almost all of the left kidney and stomach and part of the lower lobe of the left lung. The doses used are above renal tolerance and could not be given to both kidneys. Hypertension in some individuals would result from vascular damage to the kidney. Pulmonary fibrosis in a portion of the left lower lobe would also be expected although generally of no clinical significance. Also radiating the stomach is more apt to produce nausea and vomiting, although the risk of long-term effects is very low at the doses used. Removal of the spleen also enables one to treat the paraortic and pelvic nodes in one field if disease is present below the diaphragm. Otherwise, the treatment field is too large for the patient to tolerate and must be split into two fields, one including the spleen and para-aortic nodes and the other the pelvic nodes. These would have to be treated separately requiring an additional four weeks of treatment. Thus splenectomy frequently saves that four weeks. Finally splenectomy causes a temporary increase in the blood counts and when performed subsequent to the treatment of the mantle field increases the hematopoietic tolerance to abdominal irradiation. The hematologic effects of splenectomy may also make subsequent chemotherapy easier.

In order to derive the maximum benefits from this surgical procedure, it is essential to coordinate the activities of the surgeon, radiation therapist, diagnostic radiologist and chemotherapist. The surgeon must know which if any nodes are suspicious or positive on the lymphangiogram so that he can biopsy the correct one. It is also our practice to have the radiation therapist present in the operating room so that he has a clear understanding of the extent of abdominal disease and the position of the silver clips outlining any disease.

IV. Repositioning of Ovaries

When it is necessary to irradiate the pelvic lymph nodes in women, the ovaries in their normal position would receive the full dose of 3500-4500 rads as they lie too close to the nodes to shield. This dose is more than enough to ablate ovarian function. A simple operation has been devised by Trueblood to move the ovaries to the midline where they may be shielded from approximately 90 per cent of the irradiation.[6] Preliminary results are that the hormonal function of the ovaries can be preserved about 50 per cent of the time following such a procedure. Information about childbearing subsequent to this procedure is lacking due to insufficient length of followup.

V. Histologic Classification

Hodgkin's disease has formerly been separated into three subdivisions histologically, namely, paragranuloma, granuloma and sarcoma. Recently a more detailed classification and one that is considerably more useful in separating out groups with different prognoses has been developed by Lukes and Butler.[7] This classification divides Hodgkin's disease into four histologic types: lymphocyte predominance, nodular sclerosis, mixed cellularity and lymphocyte depletion. Lymphocyte predominance includes paragranuloma and some granuloma cases. Nodular sclerosis is a type of granuloma based on the presence of collagenous bands. Other granuloma cases without collagenous bands fall into the mixed cellularity type for the most part. Lymphocyte depletion corresponds to the sarcoma cases but also includes some granuloma cases.

In general, the prognosis correlates best with the stage of the patient, and the more favorable histologic types, namely, lymphocyte predominance and nodular sclerosis tend to fall into the early stages. Even within a given stage, however, lymphocyte predominance and nodular sclerosis patients have better prognosis than patients with the histological types of mixed cellularity and lymphocyte depletion.[8] Also of interest is that there seems to be a relationship between site of origin of the Hodgkin's disease and the histological type. For example, patients with mediastinal involvement only usually have nodular sclerosis.

VI. Results of Treatment

When the patient has been staged in the manner described above, a treatment policy can then be decided upon. We would like to emphasize that all the procedures described above including laparotomy and splenectomy are necessary for accurate staging and furthermore staging directs subsequent therapy. All stage I and II patients and all stage III A patients should receive radical radiotherapy. Some stage III B patients may be suitable for radical radiotherapy as well. Radical radiotherapy consists of treatment of all known disease to a dose of 3500 rads or more with intent to cure. It has also been our practice to treat adjacent clinically uninvolved lymph node areas as well.

The clinical course of stage I and II patients treated with radical radiotherapy was reported by us in 1969.[9] At that time, length of followup of treated stage III patients was not sufficient for us to include them in the report. It must be emphasized that some of these patients did not have lymphangiography and none underwent laparotomy for staging. Figure 1 describes the survival of such patients. At 5 years, 82 per cent are alive and 55 per cent are living and free of disease. The latter are presumably cured since the flattening of the curve indicates no new disease developing in these patients beyond five years. In a group of stage I and II patients not treated radically, the 5-year survival was 35 per cent. None of these survivors was free of disease and all have subsequently died. These survival data compare favorably to results obtained by other investigators in patients with stage I and II Hodgkin's disease similarly treated. Five year survival rates of 55 per cent, 65 per cent and 55 per cent have been reported by Kaplan,[10] Peters[11] and Easson.[12]

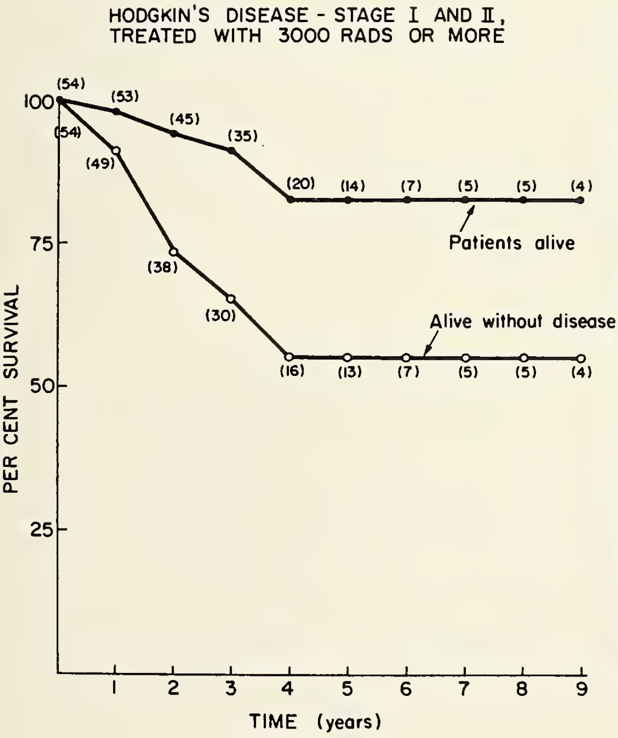

Figure 1

Cumulative survival rates in patients with stage I and II Hodgkin's disease treated with radical radiation therapy. The upper curve includes all patients. The lower one eliminates those living with disease at the time of the first reactivation. The numbers in parentheses represent the number of patients at risk.

In our 1969 report,[9] we attempted to learn more about the reasons for failure among the 45 per cent of patients treated radically who are not cured. It became apparent that direct extension of disease to the abdomen was fairly common following initial treatment to nodal areas above the diaphragm. Furthermore, patients who developed new disease within the abdomen following chest (mantle) irradiation had a very poor prognosis. Abdominal extension may be followed in a short time by widespread dissemination. Thus it is important to detect abdominal disease in its early stages. This is why we have placed such emphasis on the procedures of lymphangiography, laparotomy and splenectomy.

VII. Current Treatment Policies

The staging procedures described in section II are first carried out, with the exception of laparotomy. If the patient appears to be stage I A, II A or III A, the mantle portal is first treated (Fig. 2), 3500 rads in 3½-4 weeks being delivered to the whole portal and an additional 1000 rads being added to

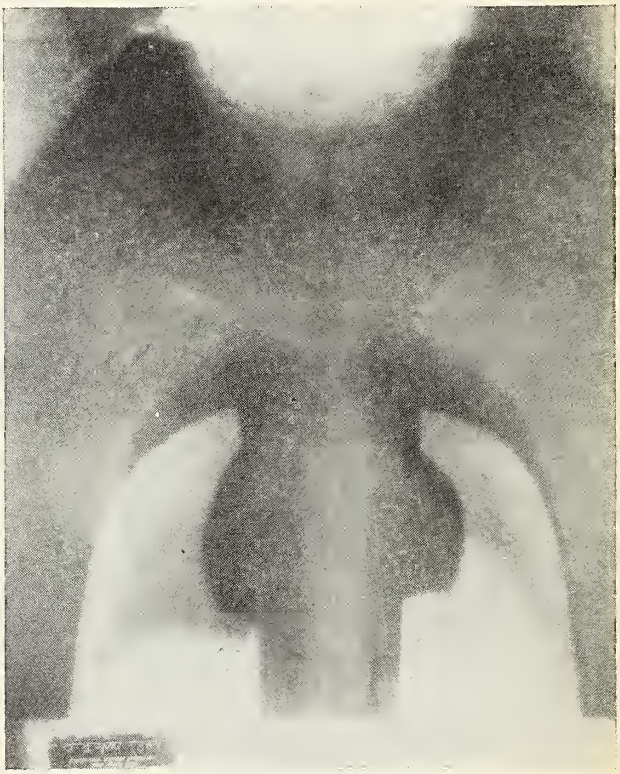

Figure 2

Port film showing the supradiaphragmatic field of irradiation (mantle portal) covering lymph node areas above the diaphragm and including the mediastinum, hilar areas, infraclavicular and supraclavicular nodes, axillary and cervical regions up to the mastoid. The lungs are spared by individually shaped lead blocks (shown in white). This film is taken with the patient in the treatment position on the 6 Mev linear accelerator.

the areas of known involvement. Laparotomy and splenectomy are then performed. If disease is found within the abdominal nodes but not in the liver, all the para-aortic, pelvic and inguinal nodes are then treated (Fig. 3). This starts as soon as practical after the laporatomy, usually about two weeks. Again the dose delivered is 3500 rads to all the nodes and 4500 rads to the grossly involved areas, all at a rate of 800-1000 rads weekly. Care must be taken to separate the chest and abdominal fields on the skin so as to not overlap the fields within the patient.

If disease is not found in the abdomen, the para-aortic nodes only are treated prophylactically. We also elect to treat the pelvic nodes in certain patients with negative explorations if the lymphangiogram is equivocal because of the limited sample of nodes that is obtained at surgery. Frequently nodes that are not grossly enlarged may be quite difficult to find at operation.

In patients who appear to be stages I B, II B and III B, the laparotomy is done first to be certain of the stage before proceeding further. Patients who are stage I B or II B postoperatively are candidates for radical radiotherapy and are treated the same way as I A and II A patients. First the chest is irradiated and then the abdomen. Following irradiation of the mantle field, a 2-3 week break may be necessary to allow for bone marrow recovery before beginning para-aortic irradiation.

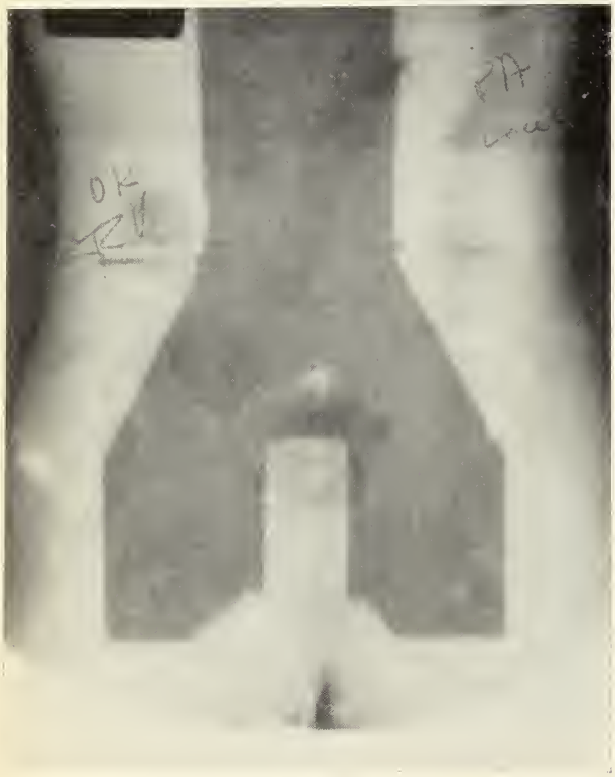

Figure 3

Port film of inverted Y field used for infradiaphragmatic disease including para-aortic nodes, splenic pedicle, iliac and inguinal nodes. The upper portion of the field cannot be seen as it is too large for one film. The film is taken with the patient in the treatment position on the 6 Mev linear accelerator.

In women of childbearing age or younger in whom one wishes to preserve ovarian function the ovaries may be moved to the midline in patients with involvement of abdominal nodes. This may be done at the time of the initial laparotomy in patients with obvious disease in the abdomen, although a second suprapubic incision is required. Final histologic diagnosis on the status of the abdominal nodes will generally not be available for several days and it may occasionally be necessary to bring the patient to the operating room a few days after the laparotomy to move the ovaries.

Patients who are stages III B and IV are primarily candidates for chemotherapy. Some stage III B patients may be curable with radical radiotherapy. We have endeavored to select out these patients by arbitrarily setting the following criteria for those to be treated by radical radiotherapy: (1) The histology must be lymphocyte predominance or nodular sclerosis, (2) Only one of the three symptoms of fever, night sweats or itching may be present, (3) No other symptom or sign such as anemia, weight loss or malaise may be present. Those who do not meet these criteria are treated with combination chemotherapy and low dose radiotherapy. This program is described in detail by Dr. DeConti elsewhere in this symposium.

VIII. Conclusion

Our concepts about Hodgkin's disease are in the process of a rapid evolution. What we think should be done today could change tomorrow. Although once considered to be universally fatal, it is now clear that the disease can be cured with appropriate radiotherapy. The required diagnostic techniques and subsequent therapeutic procedures are long and complex. It is probably wisest after the diagnosis has been established to refer patients with Hodgkin's disease to a medical center experienced in its management. It is unacceptable that such patients should, without further evaluation, receive initially palliative treatments, either in the form of localized low dose radiation or systemic chemotherapy. Not only may this needlessly delay the undertaking of proper treatment and perhaps allow the disease to progress to a stage which is no longer curable, but also preliminary treatments may themselves seriously interfere with subsequent curative attempts even in early stages of the disease.

While this entire program may seem, and in fact is, both time consuming, difficult and expensive, the success achieved in the treatment of Hodgkin's disease justifies the effort. With sophisticated radiotherapy techniques the incidence of complications is low and seems to be a minimal price to pay for the enormous improvement in the outcome of this once universally fatal disease.

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New Film on Alcoholism

Physicians involved in presenting educational programs on alcoholism for civic organizations might be interested in literature on a new film entitled "Alcoholism Disease In Disguise." The twenty-seven minute film, in color, covers the complex disease problems of the chronic alcoholic. The "cast" includes psychiatrists, internists, social workers, pathologist, a GP, and an AA official.

The film was produced by Ayerst Laboratories of New York and is distributed by Association Films. For the convenience of Connecticut physicians, the film may be ordered through Leonard R. Tomat, Assistant Executive Director for Educational and Scientific Activities, 160 St. Ronan Street, New Haven, Conn. 06511.

The Yale Combination Chemotherapy Program For Advanced Hodgkin's Disease

A Preliminary Report

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Introduction

Optimum treatment of Hodgkin's disease requires the specialized skills of surgery, X-ray therapy, and chemotherapy. Improved diagnostic techniques have permitted more precise anatomic staging of disease, and specific roles have been defined for the therapeutic modalities depending upon the extent of disease. The purpose of this paper is to review the rationale for and to present some preliminary results of a new combination chemotherapy program for stage IIIB and IV Hodgkin's disease.

Several theoretical considerations have contributed to the development of combination chemotherapy. Among these is the concept of utilizing a combination of agents each with different host tissue toxicities, to achieve an additive effect on tumor tissue without prohibitive host toxicity.[1] At a more fundamental level, knowledge concerning the biochemical mechanisms of action of antineoplastic agents and the kinetics of tumor cell growth have provided additional theoretical approaches to the development of effective combination therapy. At the biochemical level,[2] combinations of drugs may be selected to act at the same receptor or enzyme site or to affect different biological processes in the target cell. Kinetically, it has been shown that the susceptibility of cells to cytocidal effects by antimetabolites is proportional to their growth rate.[3-5] This circumstance provides a theoretical basis for the sequential therapy of a tumor with a non-cycle-specific agent such as an aklylating agent followed by a cycle-specific drug (e.g., an antimetabolite) once the surviving cells have recommenced logarithmic replication.[6, 7]

In a recent review, Henderson and Samaha[8] compared rates of complete remission in Hodgkin's disease achieved by single versus combination drug chemotherapy. Single drug series employing either vincristine,[9] cyclophosphamide,[9] prednisone,[10] methotrexate[11] or procarbazine[12, 13] produced complete remission rates ranging from 8 to 58 percent with a mean of 26 percent. In contrast were three series[14-16] of patients who received combination therapy and underwent complete remission rates from 63 to 81 percent with a mean of 72 percent. The response durations varied from 2 to >7 months for all single drug regimens. Those for the 3 combination programs were 4-12, >20, and >32 months.

The current protocol was designed with the concepts outlined above in mind. The drug schedule includes all of the maximally effective drugs in a sequential-combination schedule.

Methods and Materials

Patients

Patients with stage IIIB or IV disease, previously untreated with chemotherapy, or patients who had relapsed after radiation therapy were included in the study. Staging procedures included lymphangiography, metastatic X-ray series where indicated,

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complete blood counts, bone marrow biopsies, renal and liver function tests (blood urea nitrogen, serum creatinine, serum uric acid, serum alkaline phosphatase, SGOT, LDH, and serum bilirubin), and liver biopsy if indicated. All patients had histologically confirmed disease. More recently laparotomy and splenectomy have been added to aid in clinical staging and in treatment as described in Dr. Nuland's report.[17] The characteristics of 19 patients entered from February 1969 to March 1970 are described in Table 1.

Plan of Drug Treatment

The original treatment plan consisted of 3 cycles of therapy, each of 2 months' duration (Figure 1). On the first day of therapy, a rapid intravenous infusion of nitrogen mustard (mechlorethamine-HCl) in a dose of 0.4 mg/kg of body weight was administered. This was usually carried out in the evening in fasting patients premedicated with 100 mg of secobarbital and 15 mg of prochlorperazine. On the following day and at weekly intervals for a total of three doses, vincristine, 1.4 mg/M² body surface was given intravenously. Prednisone was also started the day after nitrogen mustard. Fif-

Figure 1

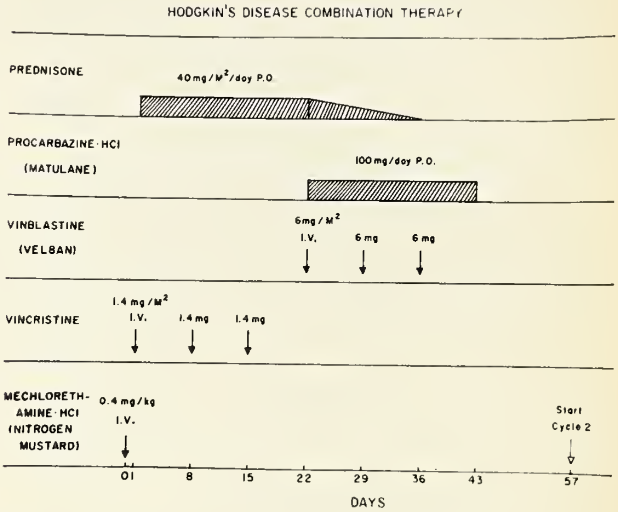

TABLE 1

RESULTS OF COMBINATION CHEMOTHERAPY IN PATIENTS WITH HODGKIN'S DISEASE

Patient	*Age*	*Sex*	*Stage*	*Predominant Site*	*Previous X-Ray Therapy*	*Response*	*Remission Duration*
C. N.	60	F	IIIB	Spleen	0	complete	21 weeks
S. D.[1]	59	F	IVB	Liver, bone	+	none	—
H. G.	35	M	IVB	Liver, lungs	+	complete	61+
P.B.	37	F	IVB	Liver	+	complete	49+
A. S.	30	F	IVB	Spleen, thymus	+	complete	35+
C. J.[2]	19	M	IVB	Gut	0	complete	29+
J. G.	46	M	IIIB	Nodes	+	complete	16+
W. L.	30	M	IIIB	Nodes	0	complete	24+
S. O.	15	F	IVB	Pleura	+	complete	34+
C. D.	15	F	IVB	Liver, spleen	0	partial	25+
J. B.[3]	13	F	IVB	Spleen, pelvic	0	partial	22+
C. T.[4]	13	F	IIB	Nodes	+	complete	21+
T. M.	48	M	IVA	Nodes	+	complete	3+
A. B.[5]	52	M	IVB	Nodes	+	complete	2+
L. M.[6]	42	M	IVB	Liver, nodes	+	complete	31
J. G.[7]	25	M	IVB	Spine	+	partial	47+
J. H.[8]	37	M	IIIB	Nodes, Spleen	+	complete	2+
A. L.[9]	19	M	IIIA	Spleen	+	partial	2+
E. F.[10]	34	F	IVB	Liver, spleen	+	complete	11+

[1] Died one week after commencing therapy of sepsis and pulmonary emboli unrelated to chemotherapy.

[2] Pre-chemotherapy surgery for Hodgkin's mass in cecum.

[3] Prior steroid therapy for erythema nodosum.

[4] IIB. Recurrent mediastinal mass after "maximal" radiotherapy.

[5] Prior chlorambucil, vincristine, velban.

[6] Previous nitrogen mustard and vinblastine.

[7] Previous vinblastine.

[8] Splenectomy, IIIA.

[9] Splenectomy.

[10] Prior intrapleural thiotepa, prednisone, splenectomy.

teen days after the start of therapy, the second half of the cycle was initiated if recovery from hematologic depression had taken place (vide infra). This part of the cycle consisted of a combination of procarbazine (100 mg/day, orally) for 3 weeks together with weekly vinblastine for 3 doses. After the completion of the cycle 2 weeks were allowed for bone marrow recovery, and the cycle was repeated. Prednisone was omitted from cycle 2 to minimize steroid toxicity.

This program has recently been modified to include subsequent irradiation of initially diseased regions; this to be followed by two further cycles of chemotherapy at 3-month intervals. Thus, the original protocol was designed to have a duration of approximately 6 months while the revised regimen requires approximately 1 year for completion. Most of the patients to be described in this communication received therapy according to the original program.

Drug Dose Attenuation Guidelines

Therapy was modified according to defined levels of toxicity. The vincristine dose was halved for mild neurologic toxicity such as loss of deep tendon reflexes or mild paresthesias; for more severe neurologic toxicity, doses were eliminated for the duration of neurotoxicity and halved in subsequent cycles. Nitrogen mustard, 0.4 mg/kg was given if granulocyte and platelet counts exceeded 1500 and 150,000 per cubic millimeter respectively and was otherwise withheld. Vinblastine was withheld if the granulocyte count was less than 750/cu mm or the platelet count was less than 50,000/cu mm. The dose was decreased to 4 mg/M^2 if the granulocyte count was between 750 and 1500/cu mm or if the platelet count was between 50,000 and 100,000/cu mm. Procarbazine was withheld if the granulocyte count was less than 1000/cu mm or platelets were less than 50,000/cu mm. Any of the manifestations of severe steroid toxicity (peptic ulcer, severe diabetes, osteoporosis, psychosis) was considered an indication to discontinue prednisone.

Results and Discussion

The sequential combination program as outlined proved to be safe and effective. The use of vincristine, prednisone and nitrogen mustard in the first half of the cycle produced marrow toxicity no greater than that expected from the alkyating agent alone, although all drugs were used in full dosage. The second half of the cycle consisting of procarbazine and vinblastine was also well tolerated, but reduced levels of these drugs were necessary since the myelotoxicity of these drugs is additive.

Eighteen of the nineteen patients entered were able to complete at least a single cycle of therapy. The male: female ratio was 10:9 with an age range of thirteen to sixty years. All but 6 of the patients had stage IV disease (without laparotomy) and only 1 of the 19 did not have constitutional symptoms. Fourteen of the patients had received prior X-ray therapy but in only one case did this include areas below the diaphragm.

All eighteen patients who completed at least a single cycle of therapy achieved at least a partial response (>50% reduction in detectable disease bulk) and 14 of 18 (78%) experienced complete remission with disappearance of all detectable parameters of disease. At the time of writing only two patients had relapsed; one of these patients (C.N.) had a recurrence of splenomegaly one month after the termination of chemotherapy; the other (L.M.) had received previous chemotherapy. Remission durations of the other sixteen patients were calculated from the earliest date of maximal response. The mean and median durations are at least 24 and 23 weeks respectively. Table 2 summarizes the results of this program as of 6/1/70.

TABLE 2

OVERALL REMISSION RATE IN ADVANCED HODGKIN'S DISEASE

Entered	19
Early Deaths	1
Evaluable	18
Remissions	18
Complete	14
Partial	4
Relapses	2

The regimen was well tolerated and in no case was responsible for either the death of or life-threatening toxicity in a patient. With the exception of nitrogen mustard infusions, virtually all aspects of the protocol were completed on an outpatient basis while the patients for the most part continued their usual daily activities.

Drug associated toxicity was reviewed in 14 of the 18 patients where sufficient data were available. Each drug was associated with tolerable toxicity. Nitrogen mustard infusions resulted in significant marrow toxicity (<1500 WBCs, <100,000 platelets) in 36% of cycles but these were transient and not associated with significant hemorrhage or infection. Vincristine was relatively well tolerated in the pediatric age group but almost routinely caused paresthesias and areflexia in adults. Significant motor deficits did not occur and only one patient reported severe constipation as a manifestation of autonomic toxicity. Reversible alopecia occurred in two patients. Prednisone therapy was generally well tolerated although proximal myopathy and fluid accumulation were recorded by several investigators and in one case aggravation of diabetes mellitus was observed. Myelotoxicity occurred as expected during the vinblastine-procarbazine phase of therapy. This phase of the regimen was associated with significant myelotoxicity as defined above in 30% of cycles. The percentage of courses requiring dose attenuation resulting from the established guidelines is summarized in Table 3. There was no difference in the incidence of drug attenuation between the patients who had received X-ray therapy previously and those who had not; however, only one patient had radiation therapy that included both supra-and sub-diaphragmatic areas, and indeed at least one other study has concluded that previous x-irradiation does significantly hamper subsequent chemotherapy administration.[18]

TABLE 3

PERCENTAGE OF CYCLES COMPLETED WITHOUT DOSE ATTENUATION FOR EACH DRUG

Cycle *Drug* *Number of Cycles*	*(1)* *14*	*(2)* *12*	*(3)* *8*	*(4)* *2*
Nitrogen mustard	100	100	100	100
Vincristine	78	50	75	100
Prednisone	93	—	88	—
Vinblastine	28	42	38	50
Procarbazine	78	92	75	100

Summary

A 5 drug combination chemotherapy program has resulted in a rate of remission induction of 100%, including 78% complete remissions in a group of patients with advanced Hodgkin's disease. All but two patients have continued in remission, with a median duration of at least 23 weeks overall. Because of the sequential nature of the program and the guidelines for attenuation of therapy, toxicity and morbidity have been well controlled and the regimen has been well tolerated. This regimen is comparable to the best thus far described for induction of complete remissions in Hodgkin's disease; however, it is too early to assess the more important goal of therapy of this disease i.e., extended remission duration and prolongation of life. It is hoped that this program by continuing therapy long into remission will succeed in reducing tumor cell numbers to levels compatible with greatly increased remission duration.[19] Although these preliminary results are very encouraging, further experience with this program and a longer follow up is necessary to define the long-term results of this program. The extension of this protocol to include further radiation therapy and chemotherapy cycles was prompted by these initial encouraging results with the objective of securing remissions of maximal duration.

Acknowledgements

We are indebted to Drs. Roland T. Skeel and Leonard Farber and all the physicians who participated in the care of these patients and the staff of Hunter 5 for excellent supportive care, in particular Mrs. S. Blood, R.N., and Mrs. C. Burhenn, R.N. We also thank Mrs. S. Hubbard, R.N., for her assistance in reviewing and collecting the data.

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Old socks want much patching.

Of young men die many,

Of old men escape not any.

Old men go to death, but death comes to a young man.

The old man's staff is the rapper at Death's door.

They who would be young when they are old must be old when they are young.

To the old, of a molehill he makes a mountain.

The young man knows the rules, but the old man knows the exceptions.

—*Oliver Wendell Holmes*

Connecticut Medicine

Editorials

The Outlook For Control Of Acute Respiratory Tract Disease

The impact of respiratory viruses and mycoplasma pneumoniae today is essentially what it was several decades ago. Influenza viruses continue to ravage this country and other parts of the world. For example in 122 cities of the United States, 26,000 excess deaths were attributed to influenza A2 virus in 1957-58 and 19,500 to Hong Kong A virus in 1968-1969. Frequent shifts in antigenic structure of Influenza A and the need for yearly injection of vaccine even in the absence of antigenic variation have limited the effectiveness of licensed commercially produced influenza vaccine. Control of other respiratory agents which is a cause of the major proportion of acute diseases of the respiratory tract promises to be a task more formidable even than the prevention of influenza virus infection.

Some difficulties that must be overcome are the multiplicity of agents, for example, one mycoplasma species and 118 distinct viruses, belonging to 7 different virus groups. Then there is the variation in pattern of disease produced by different agents, a spectrum of effects which range from mild upper respiratory tract infection to serious pneumonitis. Other difficulty is change in prevalence and host immunologic factors. Finally, is the question of safety of vaccines. Two major causes for concern have been found to be altered reactivity or sensitization to subsequent naturally acquired infections and a threat more ominous than sensitization—namely, oncogenicity, although this danger has not materialized thus far. The fear arose from recognition that several human adenovirus serotypes induced sarcomas when injected into newborn hamsters.

There are now recognized two types of antibody that determine resistance to infection and illness. One type is in the serum and this mediates immunity for those viruses that undergo a systemic phase of dissemination such as the adenovirus. The other type is mediated primarily by antibody which is present in secretions such as influenza A virus infection in which serum antibody is relatively ineffective. The local antibody is in the right place to intercept viruses which attack the respiratory tract epithelium. This local IGA antibody appears to be synthesized in the plasma cells located beneath the mucosal epithelium. Thus the secretory antibody system is distinct from the serum antibody system both in site of synthesis and in type of immunoglobulin produced.

In man local respiratory tract antibody appears to be of major importance in providing resistance to type I parainfluenza virus, RS virus and rhinovirus infection. On the other hand adenovirus can be controlled by raising serum antibody. Thus it produces a type of infection different from that produced by myxo and rhinovirus. It may be that adenovirus infections penetrate to a deeper level than the more superficial myxo and rhinoviruses. This idea is supported by such features as latency, prolonged shedding, and lymph node involvement.

This basic idea about immunologic determinants has led to production of vaccines of a different kind. Since respiratory tract antibody

THE COVER

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THE Father of Psychiatry, French physician Philippe Pinel, in 1795 ordered chains and fetters removed from insane women in the Sâlpetrière, large Parisian hospital. Two years earlier, he had similarly unchained insane men in the Bicêtre. Despite political and medical opposition and uncertainties of the French Revolution, Pinel persisted in replacing cruelty and inhumanity with kindness, understanding, and rational therapy. His success in curing and relieving patients suffering from mental diseases opened new perspectives for psychiatric research and practice.

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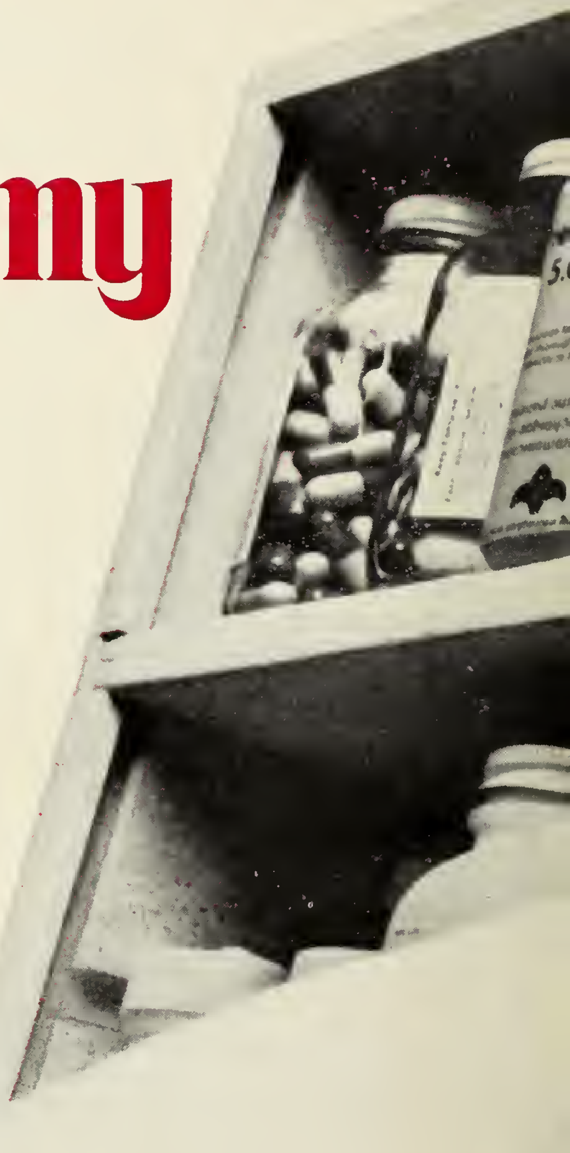

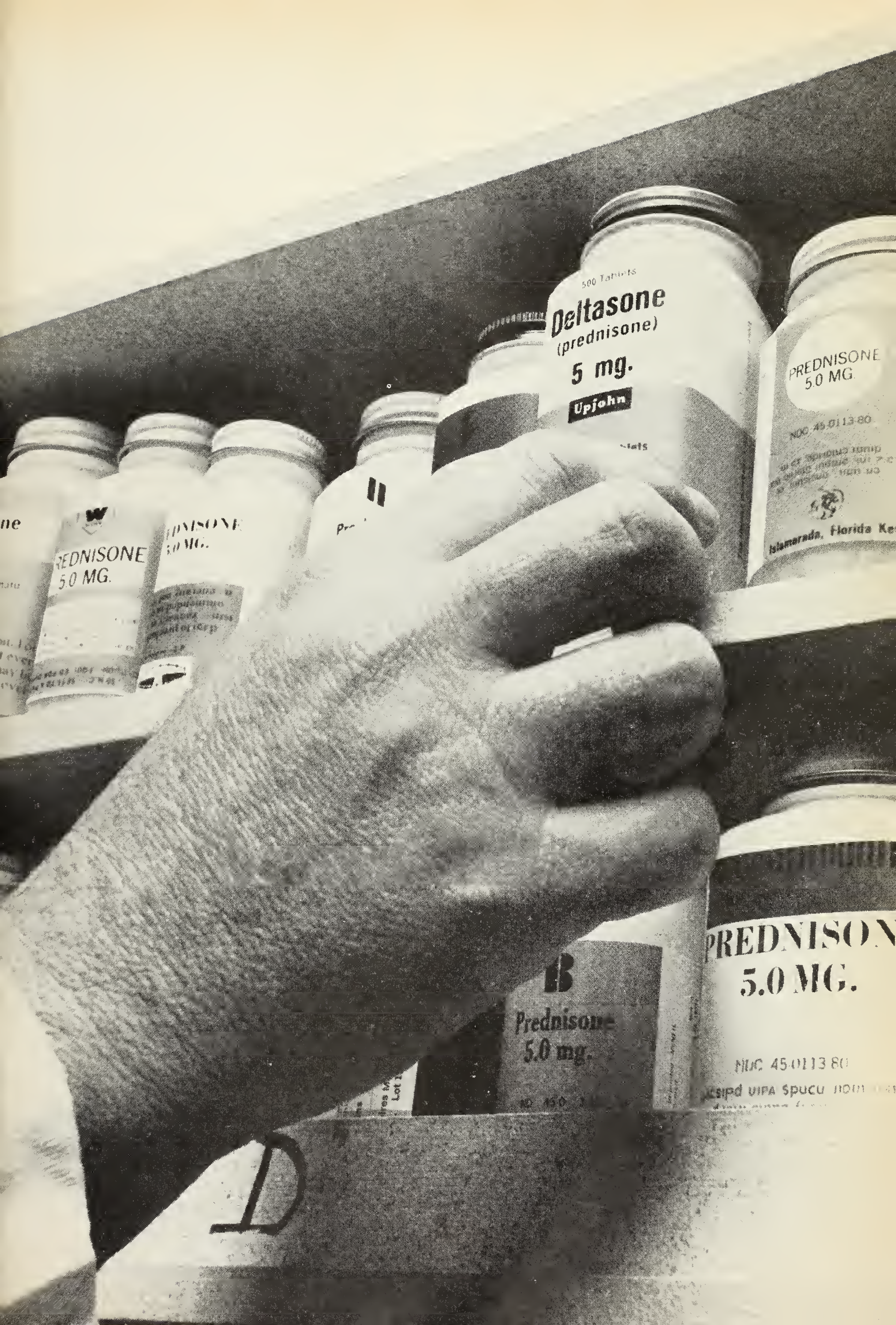
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The potency of prednisone exceeds cortisone in glucocorticoid and anti-inflammatory activity by about five times on a weight basis, but is considerably less active than cortisone in mineralocorticoid activity.

Indications are the same as those for other anti-inflammatory steroids. Representative uses include collagen diseases, allergic diseases, generalized dermatoses, acute ocular inflammatory disease, certain lymphatic neoplastic diseases, ulcerative colitis and nephrosis. *Important:* Prednisone, like cortisone, is a potent therapeutic agent influencing the biochemical behavior of most, if not all, tissues of the body. Because it manifests little sodium-retaining activity, the usual early sign of cortisone overdosage (i.e., increase in body weight due to fluid retention) is not a reliable index. Hence, recommended dose levels should not be exceeded, and all patients should be under close medical supervision. All precautions pertinent to the use of cortisone apply to Deltasone (prednisone).

Contraindications: As for all other corticoids. *Considered Absolute*—herpes simplex keratitis, acute psychoses and latent, healed or active tuberculosis. May be lifesaving in certain cases of pulmonary or meningeal tuberculosis, but should be used only in conjunction with adequate and effective antituberculous therapy to which causative organisms are shown to be sensitive. *Considered Relative*—active or latent peptic ulcer, Cushing's syndrome, diverticulitis, fresh intestinal anastomoses, osteoporosis, renal insufficiency, thromboembolic tendencies, psychotic tendencies, diabetes mellitus, hypertension, local or systemic infections including vaccinia, varicella and other exanthematous diseases, and fungal infections, and, pregnancy particularly during the first trimester because of observation of fetal anomalies in experimental animals. If necessary to give corticosteroids during pregnancy, watch newborn infants closely for signs of hypoadrenalism and institute appropriate therapy if signs appear.

If corticoids are used in the above conditions, weigh risks against benefits.

Precautions: Deltasone should be given only with full knowledge of characteristic activity of and varied responses to corticoids. Because of inhibiting effect on fibroplasia, corticoids may mask signs of and enhance spread of infection; hence, watch patients closely, and if intercurrent infection occurs, control with appropriate antibacterial measures. If possible, avoid abrupt cessation of corticosteroid therapy because of the danger of superimposing adrenocorticoid insufficiency on the infectious process. Prolonged hormone therapy usually causes a reduction in the activity and size of the adrenal cortex. When discontinuing therapy, relative adrenocortical insufficiency may be avoided by gradual reduction of dose. However, a potentially critical degree of insufficiency may persist asymptomatically for some time even after gradual discontinuation of adrenocortical steroids. Therefore, if a patient is subjected to significant stress, such as surgery, trauma, or severe illness while being treated, or within one year (occasionally up to two years) after treatment has been terminated, hormone therapy should be augmented or reinstituted and continued for the duration of the stress and immediately following it. Since mineralocorticoid secretion may be impaired, salt and/or desoxycorticosterone should be administered conjunctively. It is preferable to use a soluble hormone preparation in the immediate preoperative and postoperative periods.

Although unlikely with Deltasone, average and large doses of corticosteroids can cause elevation of blood pressure, salt and water retention and increased potassium and calcium excretion. Dietary salt restriction and potassium supplementation may be necessary. Glucocorticoid steroids may aggravate diabetes mellitus so that higher insulin dosage may become necessary or manifestations of latent diabetes mellitus may be precipitated. Corticosteroids may aggravate myasthenic symptoms in myasthenia gravis and should be given with proper precautions.

Muscle weakness, in some instances, attributed to hypopotassemia, has been reported following prolonged systemically administered corticoids. Excessive potassium loss, like excessive sodium retention, is not likely to be induced with effective maintenance doses of Deltasone (prednisone), however, keep this effect in mind and perform periodic serum potassium determinations in patients on prolonged corticoid therapy. Muscle weakness occurring with normal serum potassium levels may be due to disturbance in muscle metabolism. Severe myopathy is associated with substantial doses of steroids for prolonged periods, and evidence indicates it occurs more frequently with 9-alpha-fluro steroids. Replacement with non-fluorinated steroid has, in some instances, resulted in improvement.

Retardation of linear growth, roughly proportional to dose, has been noted in children on corticoids for six months or more. Following cessation of therapy, growth rate may be accelerated. Therefore, carefully observe growth of children on prolonged corticoid and if growth is retarded, reduce dose sufficiently to permit recovery before epiphyseal closure. Make every effort to avoid corticoids during pregnancy, since spontaneous remission of some diseases such as rheumatoid arthritis may occur. Long term corticoid therapy may evoke hyperacidity or peptic ulcer, therefore, as prophylaxis, an ulcer regimen and antacid are highly recommended. Take X-rays in peptic ulcer patients complaining of gastric distress, and, whether or not changes are noted, an ulcer regimen is recommended. Since prednisone causes less salt and water retention than many other glucocorticoids, patients should be observed closely for development of undesirable hormonal effects that are less obvious indications of steroid toxicity than edema and hypertension due to salt and water retention. Continued supervision of patients after cessation of therapy is essential, since there may be a sudden reappearance of severe disease manifestation.

Adverse Reactions: Adverse reactions associated with use of corticoids include: Cushing's syndrome, moon facies, supraclavicular fat pads, hirsutism, striae and acne; relative adrenocortical insufficiency particularly in time of stress due to trauma, surgery or severe illness; protein catabolism with negative nitrogen balance; electrolyte imbalance; alteration of glucose metabolism with aggravation of diabetes mellitus including hyperglycemia and glycosuria; osteoporosis reversible only with difficulty; spontaneous fractures; aseptic necrosis of the hip and humerus; activation and complication of peptic ulcer including perforation and hemorrhage; aggravation or masking of infection; increased blood pressure; convulsions; petechiae and purpura; menstrual irregularities including amenorrhea, spotting or prolonged bleeding; insomnia; psychic disturbances especially abnormal euphoria; nervousness; posterior subcapsular cataracts occasionally requiring extraction; increased intraocular tension; increased intracranial pressure with papilledema (pseudotumor cerebri); pancreatitis; necrotizing angiitis; thinning of scalp hair; suppression of growth in children; thromboembolic complications; facial erythema; allergic skin reactions; ulcerative esophagitis; sweating; vertigo; weakness; myopathy; headache; exophthalmos. Adverse reactions are usually reversible and usually disappear when drug is discontinued.

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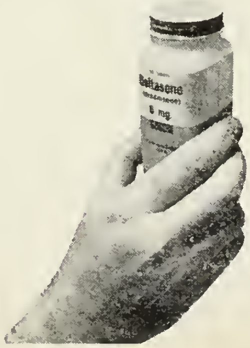

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plays such a decisive role in resistance, efforts to induce immunity are now directed to stimulation of production of local antibody. This type of immune response can be induced more efficiently and more frequently by direct introduction of either live or inactivated antigen into the nasopharynx. The superiority of direct introduction of antigen was demonstrated by Chanock[1] and others and so our most pressing need at present to control respiratory tract virus infection is not by conventional parenteral vaccines, but by materials which will enhance and prolong the production of local respiratory tract antibody.

Chanock[1] has just described his experiments. The RS virus is the most important respiratory tract pathogen of early life. He attenuated the virus by successive passages in bovine embryonic kidney tissue. After 52 passages the virus exhibited decreased infectivity and lack of virulence when tested in 45 adult volunteers. Parainfluenza virus infections are not controlled by inactivated virus instilled in the nasopharynz. However, rhinovirus infections can be controlled by intranasopharynx instillation of inactivated vaccine. This mode of vaccine administration is simple and the approach could be expanded to provide protection against a multitude of serotypes which together cause most of the common cold illnesses in older children and adults.

The adenovirus which can be controlled by a high titer of serum antibody was conquered by a different approach than nasopharynx instillation. These viruses cause large scale epidemics of acute respiratory disease in military recruits. In such an ideal setting for study, Chanock gave type 4 virus in an enteric coated capsule to adult volunteers. A selective infection of the lower gastrointestinal tract occurred. It was asymptomatic but stimulated the development of moderately high levels of serum neutralizing antibody. Furthermore no spread of the infection took place to non infected individuals and no respiratory tract disease resulted. It was then given to several hundred thousand military recruits without evidence of any outward effect but with complete protection against respiratory tract disease. Following this protection a new type 7 emerged but this was also controlled by enteric capsules containing the virus. Now a capsule containing both type 4 and 7 is available for eradication of both viruses.

A mycoplasma pneumonia vaccine is urgently needed. Its incidence is high in children and young adults. It has a prolonged course and does not yield to tetracycline or erythromycin. Presently protection by inactivated vaccine is not great. Furthermore, attempts to develop a satisfactory attenuated live vaccine have been unsuccessful thus far.

Despite the difficulties that exist the outlook for eventual control of acute respiratory tract disease is encouraging. The biology and ecology of the respiratory tract pathogens are reasonably well understood, and within the past few years we have gained considerable insight into the immunologic determinants of resistance to infection and respiratory illness. Thus, it appears that most of the ingredients for successful immunoprophylaxis are now at hand. The next few years cannot help but be both exiciting and productive of effective respiratory tract vaccines. —L.H.N.

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Marihuana: II

Because of marihuana's widespread use, the knowledge of its adverse affects, of its addictive liability and of its relation to crime, narcotic addiction and psychoses assume great importance. Mild liver dysfunction has been found in 8 of 12 regular users by Kew[1] and three showed striking parenchymatous degeneration. No chromosomal damage was observed in human leukocyte cultures exposed to cannabis, nor in cells cultured from rat embryos. In contrast, such damage is known to occur with LSD. However, teratogenic effects have been observed[2] in rats, mice, rabbits and hamsters by injecting resin extracts early in pregnancy. Even though no case of human fetal damage has been attributable to cannabis alone, the results in animals are ominous enough to specifically caution women to avoid marihuana.

As far as addiction liability is concerned, there is general agreement that cannabis tolerance and withdrawal syndromes do not develop in humans. Observances on humans also suggest that users as they gain experience perform better with the drug. Whether there is a psychic rather than psychologic difference is not clear. Psychic dependence would be that state in which the user needs the drug to maintain his optimum level of psychologic functions, for example sexual potency or social relaxation and would suffer impaired performance or dysphoric feelings without it. No one knows the answer to this. But there seems little doubt that marihuana has the potential to serve as substitute gratification and in this sense does produce psychic dependence.

There is a huge and opinionated literature as to whether chronic marihuana use influences psychologic functioning, leads to crime or narcotic addiction or even to psychosis, whether they are insidious effects on the personality that tends to diminish intelligence, motivation or effectiveness in work and study. Pillard[3] points out the methodologic difficulty in arriving at acceptable answers. Obviously what we need is a method to asses the presence of marihuana in body fluids after which it will be possible to assemble evidence on its association with crime, auto accidents, etc. At the present, the most consistant summary of animal and human research indicates that intoxication usually decreases hostility and aggressiveness but there may be circumstances in which the reverse occurs as reported by Carlini[4] in starved rats.

Marihuana itself is not physiologically addicting, but various authors have been impressed by the frequency with which its users seem also to be indiscriminate users of LSD, amphetamines, barbiturates and heroin. If there is such a relation, does this imply that marihuana specifically predisposes to other drug use or is there some general personality trait that leads independently to multiple drug use. Some subjects have said that smoking marihuana was instrumental in their later use of LSD or heroin because they knew where illegal drugs could be obtained. On the other hand, current work at the Boston University Psychopharmocology Laboratory indicates there are personality variables associated with the readiness of a person to try drugs[5] both legal and illegal and with response to drugs when used. The strength of this association and its mechanism is not known.

Cannabis as a precipitant of schizophrenic reactions has received much attention. One is acute toxic delirium. But many authors believe chronic schizophrenic reactions or dementia lasting for months or years also result. The condition is reported most frequently from India, Morocco, and Africa where hundreds of cases have been reported, whereas only few came from the United States. The reports are extremely difficult to evaluate since they describe schizophrenic reactions in persons who also happen to be using cannabis. Some authors maintain that cannabis psychosis is difficult or impossible to distinguish uniquely on clinical grounds.[6]

Good epidemiologic studies have not been done. The relationship between cannabis and the onset of a functional psychosis is not always clear. What role did the drug play? Could the psychosis have begun without the drug? Was the use of cannabis the patient's attempt to cure his developing psychosis? These questions were asked in 1939 by Bromberg and have not been answered as of this day.

McGlothlin and West[7] believe that regular use of marihuana may very well contribute to some characteristic personality changes. Such individuals exhibit greater introversion, become totally involved with the present at the expense of future goals and demonstrate a strong tendency toward regressive thinking. They report a greater subjective creativity but less objective productivity. They seem to be subtly withdrawing from the challenge of life. These are impartial impressions and easily subject to a definitive test.

Pillard[3] surveyed a medical student population to determine correlation between use of marihuana once a week on their scholastic achievement and found no impairment. However, he did not have enough evidence from heavy users to draw any conclusions. The author thinks therefore that no one has been able to make a judgment about the "safety" of marihuana. Goode[8] points out that many of the issues go beyond the test of scientific instruments. They sum up styles of life . . . cultural perspectives . . . outlooks on the world which shape the individual's behavior.

Thus with regard to marihuana there is more to it than pharmacology, and future research must concern itself also with the individual's life style, cultural perspectives and his outlook on the world his psychologic make-up and values.—L.H.N.

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Calcium Malabsorption With Advancing Age

In osteoporosis calcium is slowly withdrawn from the bones to the amount of at least 30 mg per day, amounting to a gram per month. In 20 years the skeleton will have lost on the average of 240 grams. This loss may be attributed to either insufficient calcium intake, inadequate intestinal absorption of calcium, inadequate hemostatic balance between parathormone and calcitonin creating a persistent negative balance. Finally is the possibility of loss of collagen synthesis by the osteoblasts due to the aging process.

One of these variables, calcium absorption from the intestinal tract has just been carefully examined by Bullamore and his colleagues and reported in a recent issue of Lancet. They investigated 75 men and 115 women who were under no treatment that could affect their calcium metabolism and who had no metabolic disorder. Some were healthy, others convalescing from an acute illness. Radioactive calcium phosphate was given post-prandially and their blood tested with an automatic liquid scintillation counter. The procedure adequately reflected calcium absorption.

In men calcium absorption ranged from .3-.9 of the dose per hour up to age 60. Thereafter the absorption rate fell gradually until by the 9th decade it had fallen to .2-.4. In women below 60 the range of calcium is also .3-.9 per hour. As the age increases to the ninth decade there was a continuous fall until it had dropped to .1-.4 per hour.

Thus there seems no doubt that calcium absorption falls with age in both sexes starting at age 55 in women and 65 in men. The cause of this decline in calcium absorption might reflect a general decline in intestinal function with age. It could be specific to calcium alone, in which case it would be tempting to think that perhaps the subjects were not ingesting a sufficient amount of Vitamin D. Bullamore believes that Vitamin D may be at least a contributory factor. In Britain Vitamin D in the diet is generally low^2 about 150 IU per day, especially in elderly women.

Overt osteomalacia have been reported from scattered regions of Scotland. In view of their finding, probably many were subclinical cases of Vitamin D deficiency with malasorption of calcium exist, which have not been recognized. It appears that plasma Vitamin D in the British population is among the lowest in the world. Whatever the cause of this calcium malabsorption its significance to the pathogenesis of osteoporosis would appear to be important. If there is simple malabsorption of calcium this could be expected to lead to negative calcium balance and thus become a contributing factor in the production of osteoporosis.

One question that needs to be answered is whether declining calcium absorption in postmenopausal women can be related in any way to estrogen deficiency. This problem could be readily answered by Bullamore's technic. What is likely is that malabsorption of calcium may significantly contribute or even be responsible for the progressive loss of bone in both sexes from the age of 55 onward and which is associated with a steep rise in the incidence of collapsed vertebrae and femoral neck fractures at this time of life. In this connection, Bullamore et al did find that most old people with fracture at the neck of the femur do have malabsorption of calcium.

The calcium requirement of adults is uncertain, but has lately been set at 500 mg per day. Whether or not this is a reasonable estimate of the amount required to maintain calcium balance in normal healthy adults, it is clear that 500 mg per day requirement must also take into consideration the calcium absorptive status of the particular individual. For it may well be that a calcium intake and Vitamin D intake cannot be considered in isolation, but must be related one to the other.

In any event, in treating patients with osteoporosis, not only calcium, hormone and calcitonin must be considered, but also Vitamin D. —L.H.N.

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Drug Induced Lupus Erythematosus Syndrome

The lupus erythematosus cell phenomenon (LE) was first described at the Mayo Clinic in 1948.[1] Soon thereafter reports began to appear relating it to the administration of drugs. The first one of the many drugs implicated as the cause of a syndrome similar to systemic lupus erythematosus was hydralazine.[2] This drug-induced syndrome closely resembled the spontaneously occurring disease. At the clinical level there are some differences although on the whole they are marginal.

Lung manifestations are very common for example in the syndrome caused by procainamide. In 54 cases pleurisy was a feature in 17 (30 per cent), whereas it occurred in only 13 of 520 cases (2.5) of the spontaneously occurring disease reported by Dubois and Tisfanelli.[3] Renal manifestations which are common in the spontaneous form are very unusual in cases caused by procainamide. On the other hand in the lupus precipated by hydralazine 11 of 50 patients reported by Alarcon-Segovia et al had renal disease. Anemia had been reported in drug induced lupus but it is commoner in the spontaneously occurring form of the disease.

The drug induced form of the disease has been generally considered to be reversible on withdrawal of the precipitating agent. Nevertheless, in two series of patients with hydralazine syndrome 25 of 35 patients still had clinical manifestations up to 9 years later and a positive antinuclear factor 10 years later. Thus the difference between the naturally occurring disease and the drug induced form may not be as great as believed.

Over 150 cases of hydralazine induced lupus have been recorded and its seems that between 8-13 per cent of hypertensive patients treated with the drug will develop lupus erythematosus. It had been thought that large doses, more than 400 mg were thought necessary to produce the syndrome, but in one series of 48 patients, 15 had been taking 200 mg hydralazine per day or less and 13 developed symptoms less than 1 month after starting the drug.[4] Hydralazine is known to be acetylated in the cytoplasm of the liver cell and the population can be divided into slow or fast acetylators of hydralazine on a genetic basis. Since the LE develops more often in subjects of the slow hydralazine acetylation phenotype, slow inactivation of the drug may allow it to react with nuclear protein to a greater extent and so render it autoantigenic.

L.E. has been reported in 18 patients during treatment of tuberculosis with isoniazid. Patients in whom L.E. cells are found frequently have a positive antinuclear factor (ANF) also.[5-6] Like hydralazine isoniazid is acetylated in the cytoplasm of liver cells and a recent study[7] has shown that ANF was found more commonly in patients who acetylated isoniazid slowly.

Anticonvulsant drugs of dissimilar chemical structure (diphenylhydantoin, mesantoin, tridione, primidone, ethosuximide) have caused lupus in over 60 patients. These anticonvulsants are oxidized in the endoplasmic reticulum of the liver cells and for at least one of these drugs (diphenylhydantoin) there is known to be a range of rate of metabolism in different individuals. It would be of considerable interest, therefore, to find out if this drug induced lupus, is again commoner in patients with a slow rate of drug metabolism.

Other drugs such as sulfonamides, phenylbutazone, methylthiouracil, have also been implicated in a few cases. A recent review[7] suggests that drugs which precipitate lupus can be divided into 2 categories. One group are those drugs that produce L.E. by their peculiar pharmacological properties. In this group are hydralazine, isoniazid, anti-convulsants and procaine. A second group are such drugs which produce an allergic response. Drugs in the first category are those which are given for a prolonged period before the syndrome is produced. The second group, show other allergic manifestations frequently.

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This classification, however, is difficult to substantiate because there is overlap. For example, hydralazine when given in small doses for a period of less than a month may cause lupus, but it can also cause a positive direct Coombs' test and a positive antinuclear factor, features associated with drugs in the "allergic" group such as methyldopa.

The question then remains whether we should accept the idea that drugs will cause L.E. only in patients who are genetically predisposed and that the change in environment caused by the drug precipitates the full blown syndrome. Attempts to reproduce the phenomenon by prolonged administration of drugs to animals have thus far failed, although some serological abnormalities can be shown.[8]

Further evaluation of the drug induced lupus syndrome must depend on careful documentation of clinical cases in man and an awareness by clinicians that many drugs chemically unrelated can produce the lupus syndrome.—L.H.N.

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Androgen Function And Impotence

The usual definition of male impotence is the persistent inability to develop or maintain a penile erection sufficient to conclude coitus, to orgasm, to ejaculation. The condition may result from organic pituitary-hypothalamic or testicular disease although it is uncommon for patients with such disorders to present with a complaint of impotence. It may also complicate severe depressive illness and schizophrenia or be due to certain antihypertensive drugs or phenothiazines. In the vast majority of impotent patients however none of these factors can be implicated and their disability has usually been assumed to be of psychogenic origin.

The role of the central nervous system and the endocrine glands especially the testes in the etiology of male potency disorders has been largely neglected because of technical difficulties in assaying various hormones and their metabolites in body fluids in health and disease. Recently however animal experiments as well as observations on man have redirected attention to the important interaction of the brain, and the sex hormones in regulating libido, and copulatory behavior. In man probably some hypothalamic structure perhaps initiated and controlled by a "sex" center located deep within the temporal lobes have an important role in the production and release of sexual hormones notably gonadotropins from the anterior pituitary. In turn these influence testicular synthesis and secretion of testosterone and other C19 steriods and ultimately sexual behavior.

The technical problems of assaying C19 steroids such as testosterone, the most potent naturally occurring androgen so far known, have now been largely overcome and thus the possible role of these substances in the pathogenesis of impotence can be examined. Cooper now reports the results of a study of urinary testosterone excretion in a group of patients with impotence. Excretion of testosterone is probably the best available measure of Leydig cell function and hence of androgenic status since it is little affected by peripheral conversion of other corticosteroids.

The mean excretion of testosterone was significantly lower (45.7 μg per 24 hours) in the impotent men than in the healthy controls (73.1 μg per 24 hours). Of the 16 patients who were grouped as predominantly "constitutional" only three had testosterone excretion above the mean whereas only 1 of the 9 in the predominantly "psychogenic" group had a level below the mean. Cooper had defined these two major groups of patients presenting with impotence in previous studies. Psychogenic impotence usually occurred in young men who themselves sought help for their disorder which was of short duration and had some specific physical or psychological precipitant. The anxiety they experienced appeared to be the major cause of their subsequent impotence. All of these men still experienced sexual desire, were aroused by appropriate stimuli, continued to masturbate and had regular morning erections.

By contrast "constitutional" impotence was of insidious onset and the patients were usually attended at the insistence of their wives. Anxiety in this group appeared to be more a result of the condition than a cause or to be related to the wife's complaint. Some of these men had never achieved adequate coitus and had undergone a progressive waning of sexual activity over the years. They rarely masturbated and early morning erections were infrequent.

The lowered excretion of testosterone in the "constitutional" group may at least in part have been due to reduced sexual activity since there is some evidence that regular sexual activity and presumably regular masturbation is associated with a raised level. It is however also possible that some of these patients produced less testosterone in the first place. Some impotent men without apparent evidence of endocrine disease showed an impaired response in testosterone secretion to human gonadotrophin which stimulates the Leydig cells. Other patients in the "constitutional" impotence group might represent the lower end of the normal distribution curve for sexual activity.

Cooper has described treatment of these patients by a combination of muscular relaxation, by provision of optimal sexual stimulation, by sex education and by "psychotherapy". Such treatment was very successful in most of the patients with "psychogenic" impotence but relatively ineffective in the "constitutional" group. In view of the lowered testosterone excretion in the latter group oral testosterone therapy was tried with varying doses 15-30 mg. daily for up to 4 months. What could these failures be due to? Were the dosages inadequate? Were the receptor sites insensitive to the hormone and longer periods of administration of the hormone might make the receptor sites more sensitive?

Further studies of varying regimes of androgen medication are required particularly in the patients with "constitutional" impotence who are resistant to other forms of therapy. The elucidation of the precise role of testosterone and other androgens in potency and impotence is clearly important because of their etiologic and therapeutic implications.—L.H.N.

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Science Tools: Tubeless Gastric Analysis By The Heidelberg Capsule

Gastric acid secretion is now being measured by having the patient swallow a nasal passed gastric tube and gastric acid secretion is augmented by the histamine stimulation test. The gastric secretion is aspirated one hour before and again one hour after the administration of histamine diphosphate or betazole HCl (Histalog (Lilly) 1.5-2.5 mg. per Kg. This latter is frequently substituted for histamine as it eliminates the need of an antihistamine drug to counteract the non-gastric effects of a large dose of histamine.

The disadvantage of this method is that it requires the introduction of an indwelling nasogastric tube which patients find most disagreeable. Furthermore it is difficult or impossible to ensure complete removal of all secreted gastric juice unless continuous hand aspiration is done and this is time consuming. These objectives are largely overcome by the use of a radiotelemetering pH pill—the Heidelberg pH capsule to measure acid secretion.

Andres and Bingham[1] measured gastric secretion with the Heidelberg pill and compared the results with those obtained on the same patients by the standard aspiration test using Histalog as stimulant. The Heidelberg pH capsule contains a miniaturized radio transmitter, a pH meter and a battery enclosed in an indigestible acrylic container measuring 20-7 mm. The battery is activated by immersion in saline just before the test. The pH measuring cell consists of an external annular antimony electrode and an internal silver chloride electrode, the two being separated by a semi-permeable membrane.

The pH changes alter the output voltage of the battery which in turn controls the frequency emission of the radiotransmitter. The radiofrequencies are picked up by an antenna which is strapped around the subjects waist. It is then recorded on both a dial and graph paper in a transistorized receiver. Ordinarily the aspirated gastric juice is neutralized with 4 10 NaOH and the amount of acid is then calculated. With the capsule the pH is monitored as $KHCO_3$ is given to the patient in sufficient amounts to raise the pH to about 7 for 5-15 minutes. As soon as the pH drops to 3 more alkali is given. The number of ml of alkali to neutralize the gastric secretion equals the amount of acid secreted in milliequivalents.

To prevent the capsule from quickly entering the duodenum and to retain it in the stomach a thread is attached to it and it was determined to be in the stomach when 55 cm of the thread had passed the incisor teeth. The thread was not uncomfortable. It had the additional advantage that it could be recovered, washed, dried and reused. The subject lay on his left side but the recording could be done in the sitting position. He could also walk around between periods of recording. Saliva was of course expectorated. Basal acid secretion was measured for a 30 minute period. Histalog 2 mg. per kg body weight was then given by subcutaneous injection. The acid secretion was then measured over the next half hour.

The measurements of the 1 hour post Histalog acid secretion by the capsule method and the aspiration method were compared in 27 unselected subjects, seven with duodenal ulcer, 5 with dyspepsia without radical abnormality. Three had gastric ulcer, one had had vagotomy and pyloroplasty for duodenal ulcer, while eleven had no disease. The authors report a comparison of the acid values obtained by the capsule and those from aspiration. The capsule method gave slightly higher mean acid measurements than did the aspiration method.

There were differences, some higher and some lower with each method. Sixteen subjects showed higher secretory values with the capsule method, while eleven showed high secretory values with the aspiration method. In some the values obtained by the two methods differed significantly. Why this was so remains to be determined. Obviously the capsule method is easier on the patient causing only minimal discomfort and it is easier to do.—L.H.N.

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Amantadine In Parkinson's Disease: An Instance Of Medical Serendipity

In April 1968, a 58 year old woman with moderately severe bilateral Parkinsonism told her Doctor R. S. Schwab that three months before while taking amantadine 100 mg. twice daily to prevent influenza, she experienced a remarkable remission of her symptoms of rigidity, tremor and akinesia. These symptoms promptly returned on stopping the drug after six weeks.

Amantadine was not developed for Parkinson's disease but rather as a preventive against influenza A_2. This drug was thought perhaps to reduce the incidence of infection in individuals exposed to "Asian flu" but only if begun immediately and continued in doses of 200 mg. a day orally for 10 days. However, the drug was rated only marginally effective against influenza and has actually been under attack because of its low efficacy and high incidence of side effects.

A new chapter began in the story of amantadine when Schwab was told of his patient's experience with it. Much to the surprise and delight of her family she became more mobile, was able to do her chores more quickly and with greater facility and showed less rigidity and even less tremulousness. Careful verification of this striking phenomenon was checked with the manufacturers whose clinical research department reported no similar cases had been called to their attention. They suggested further testing with 10 patients. Upon treatment with amantadine 7 showed marked reduction in akinesia, some improvement in rigidity and even lessening tremor. No side effects were noted.

Careful verification of this striking phenomenon was begun in 163 patients in June 1968, with the result that a number of strange findings have emerged. For example the drug has no effect whatsoever in tremors unrelated to Parkinsonism or in spastic states such as those resulting from strokes. Amantadine is a stimulant but unlike the effect of amphetamines tremor is reduced. The effect resembles those of l-dopa but are not as dramatic. Interestingly enough, these two drugs are not in any way antagonistic and the combination of the two may well be synergistic thereby requiring lesser amounts of the quite expensive levodopa.

Several questions remain. It is difficult to explain the fact that amantadine potentiates side effects of belladonna-like drugs used in Parkinson's disease from minor ones such as dryness of the mouth to major ones such as hallucinations. Such side effects do not occur immediately but develop over a period of several weeks but are not seen when amantadine is used alone.

Another but saving property of amantadine is that patients do not receive increasing benefits from increasing the dosage. In fact 500 mg. may even produce convulsions and the optimum dosage appears to be the same as that used for influenza prophylaxis, 200 mg. orally per day. One additional question that needs to be answered is why some patients whose symptoms abated initially to a thoroughly acceptable level and remained at that level for several months finally had a relapse and partial return of symptoms despite continuance of the drug. Last but not least is the question why it is that discontinuance of amantadine abruptly throws some patients back into their previous akinetic state with 24 hours.

Many attempts in recent years have been made to alleviate the distressing symptoms in sufferers from Parkinson's disease. Surgical destruction of portions of the globus pallidus or the ventrolateral nucleus of the thalmus have proved highly beneficial in carefully selected patients. However, the backbone of the management in Parkinson's has continued to be drug therapy. The drugs are used either alone or in varying combinations to suit the needs of the patient including belladonna, scopolamine, diphenhydramine and others. Currently levodopa is under investigation and the results are reported to be dramatic.

The amantadine story is another example in which a chance observation has led to an advance in medical knowledge along with such classic examples as Sir Alexander Fleming's discovery of the antibacterial properties of penicillin and many others. What is remarkable in all this is that the producers of the drug had no idea it could be helpful in Parkinson's and no one yet has any idea as to why or how it works to relieve symptoms. No less remarkable is the fact that Dr. Schwab took seriously the report by his 58 year old patient who made a simple observation on herself. It is conceivable that another physician might have dismissed this patient's observation as too far-fetched to be worthy of further examination.

What it means is that we must listen to our patients and have a "prepared mind" to pursue new observations as they come along. There is medical serendipity.—L.H.N.

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The "Hard" Costs Of Air Pollution

Polluted air affects the health of human beings, of all animals and plants. It soils and deteriorates property, impairs various production processes. It raises the rate of automobile and air line accidents and generally makes living things less comfortable and less happy. Some of these effects are quite definite and measurable but most are ill defined and difficult to measure. Probably the major benefit of pollution abatement will be focused in a general increase in human happiness or improvement in the quality of life rather than on one of the specific more easily measurable categories. Nonetheless, the "hard" costs are real and at least theoretically measurable.

Lave and Seskin[1] have tried to characterize the problem of isolating the health effects. They offer quantitative estimates of the effect of air pollution on various diseases. From epidemiologic studies, episodic relationships, and a review of the literature, there is a strong relationship between bronchitis mortality and a number of indices of air pollution. If air pollution could be abated in Buffalo, a reduction in 50 per cent mortality of bronchitis would result. As regards lung cancer, the death rate is 1.56 times as high in polluted air environments as in clean ones. This ratio increased with duration of residency in the urban areas from 1.08, for less than 1 year to 2 for lifetime residency. These authors conclude also that a substantial abatement of air pollution would lead to 10-15 per cent reduction in mortality and morbidity rates for heart disease.

Having found a quantitative association between air pollution and both morbidity and mortality, the next step was that of translating the increased sickness and death into dollar costs. Mortality from bronchitis would be reduced about 50 per cent if air pollution levels were lowered to levels currently prevailing in urban areas with relatively clean air. Thus, if air pollution in major urban areas were reduced 50 per cent, then there would be a 25-50 per cent reduction in morbidity and mortality due to bronchitis. The cost of bronchitis both in terms of lost income and current medical expenses is about 530 million per year. Abatement by 50 per cent of air pollution in major urban areas would save at least 250 million to 500 million.

Approximately 25 per cent of lung cancer can be saved by a 50 per cent reduction in air pollution. This amounts to 33 million. The studies also document a strong relationship between all respiratory disease and air pollution. It seems likely that 25 per cent of all morbidity and mortality due to respiratory disease could be saved by a 50 per cent abatement in air pollution levels. Since the annual cost of respiratory disease is near 5 billion, the amount saved by a 50 percent reduction in air pollution in major urban areas would be about 1¼ billion. There is evidence that over 20 per cent of cardiovascular morbidity and about 20 per cent of its mortality could be saved if air pollution were reduced by 50 per cent. Even a saving of 10 per cent not 20 would amount to 500 million per year.

Lave and Seskin bring forward evidence that all mortality from cancer is related to air pollution and that 15 per cent of the cost of cancer would be saved by a 50 per cent reduction in air pollution or a total of 400 million per year. Not all of these cost estimates are equally certain. The connection between bronchitis or lung cancer is much better documented than the connection between all causes or all cardiovascular disease and air pollution. Nevertheless, the investigators estimate that the total annual cost in terms of increased morbidity and mortality that could be saved by a 50 per cent reduction in air pollution would be 2080 million dollars.

A final point is that these dollar figures are surely underestimates of the relevant costs. Many health effects have not been considered in arriving at these costs. For example, relatively low levels of carbon monoxide can affect the central nervous system sufficiently to reduce work efficiency and also increase the accident rate. Psychological and esthetic effects are likely to be important though they are not measureable in the "hard" cost. Then there are the additional costs associated with the effects of air pollution on vegetation, cleanliness and the deterioration of materials and buildings which have not been included in these figures. In fact Zeidberg, et al[3] believe that the annual cost of air pollution because of health effects alone would seem between 14-29 billion annually. Is society ready to pay the price?

We, of course, cannot really deal with air polution and its effects on health as a separate entity, independent of water pollution, waste disposal, and population growth. The major source of air pollution is power production which is obtained largely from burning oil, coal, gas.

With our automobiles, electric appliances, production of synthetic chemicals, fertilizers, and with our philosophy of "throw it away and get another", we are poisoning our environment, damaging our health and impoverishing our future.—L.H.N.

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The Winter Toll Of Fatal Heart Attacks

Deaths from all causes in July in England and Wales were about 40,000. In January they were about 60,000. Usually about one half of this excess is due to respiratory disease, and slightly more than a third of the excess in winter is attributable to cardiovascular disease. Particularly coronary heart disease. In the Medical Research Anticoagulants Trial, a roughly similar winter increase was noted in the incidence of well-documented non-fatal myocardial infarctions for both initial attacks and recurrences. This suggests that the winter excess mortality represents a change in the actual incidence of infarction rather than simply a higher fatality among established cases.

At present we do not know whether the winter excess deaths is due to an increase in the incidence of coronary occlusion or in the liability to infarction of myocardium that is submitted to a given degree of ischemia or in the liability to arrhythmia of infarcted myocardium. The size of the winter rise in deaths attributable to coronary heart disease is very variable, but in England and Wales in any one year it correlates strikingly with the coldness of the particular winter. This seems to suggest that cold itself is the primary determinant but it does not tell us how this effect might operate. Presumably, it could be by actual body cooling of the skin, as in wind induced attacks of angina, or of inspired air, or by some secondary influence on personal habits such as physical activity or eating.

If the relation between cold weather and coronary heart disease mortality really is one of cause and effect, than one might expect to find that the seasonal swing was less in warmer countries, but greater in very cold ones. On the other hand, any kind of a weather situation which increases the work of the heart, such as very cold weather or very hot weather in which excessive dilation of skin vessels increases the venous return, could act as an excessive burden upon an ischemic heart. There is some evidence that this is true. In the hot southern states, it seems that during heat waves deaths may actually increase.

An example of the situation in a very cold area is described by Anderson and Le Riche. They analyzed mortality statistics in Ontario where the monthly mean temperature may fall as low as —11°C. In brief, they confirm the mortality from arteriosclerosis and degenerative heart disease is higher in the winter and that it correlates with coldness. They were, however, not able to find any difference in the size of the winter peak between northern and southern Ontario, despite the more severe climate in the north. Data from Denmark and Australia were also examined and they showed a much smaller seasonal swing than appears in the British data. The authors conclude that the seasonal swing in coronary heart disease mortality may be more apparent than real. They suggest it could be explained by the effect of acute respiratory deaths being attributed to an underlying cardiovascular cause.

In relation to the Canadian data this seems a tenable hypothesis, but in relation to British experience, there are difficulties. In the first place, it is not supported by the general experience of clinicians in Britain[1] that the incidence of myocardial infarction rises in winter to a degree that is proportionately as large as that in the reported national CHD mortality rate. In England the CHD mortality is related strongly to coldness, but very little to air pollution, whereas for respiratory disease, the association with air pollution, as well as temperature, is quite clear.[3] The situation in Ontario is also different than in Britain where colder weather is associated with a much steeper rise in deaths from all causes. Whatever, it is clear that winter in Britain is more lethal than in Canada.

It is clearly possible for the inhabitants of northern Ontario to endure a severe winter without any large increase in their risk of heart attacks. The same seems not to be true of the less severe British winter. This suggests that at least one of the previously suspected factors, namely the breathing of cold air is not likely to be important in explaining the British experience. Perhaps in Britain either the habits of the inhabitants change differently in response to cold or else people suffer greater body cooling. All who have traveled both in Britain and North America will probably agree that they tend to feel a lot colder in Britain whatever the thermometer may say. It also appears that chilblains is a British phenomenon being much more common in that country than in Northern Canada or Scandinavia.

The discovery of a disease experience in two populations should be a starting point of research to uncover an explanation. One might be dampness. In terms of absolute humidity during the winter months, the dampest place is England and Wales, followed by Australia, Denmark and Ontario. There are probably others. If we are successful in establishing the mechanism for increased mortality from heart disease in the winter months, it might help us to avoid the winter toll of fatal heart attacks.—L.H.N.

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Continuing Education

To ensure that his patient receives good medical care, a physician has two challenges to meet. The first, is the challenge from within to maintain his own competence and skill. The second, is the challenge from without, which is posed by the political and economic pressures that affect the type of care his patients receive.

The challenge from within is present as long as the physician practices medicine and it must be continuously met. This can only be done by establishing a lifelong discipline of learning. There are many wells from which the physician may draw to satisfy his thirst for knowledge. Literature, refresher courses, scientific assemblies, as well as contacts with his colleagues in the community hospitals. Teaching is perhaps one of the most effective methods of learning.

Adult learning is most readily accomplished by involving learners in identifying problems and seeking means to solve them. It is not enough in determining merely whether they took part in a learning experience or even whether they liked it. If the desired learning did not occur we must take another look at the objective and method used to determine which requires change. What Carmichael[1] points out is that continuing education must be continuing self-education, not continuing instruction. The content model of teaching aids and abets passivity and dependence on teachers. What we really need is a process which fosters self-reliance and self-learning.

Program directors must recognize that there is a need to change the learner and a need to know whether the learner has actually changed. If we do not know whether the learner has learned how to use acquired knowledge and how to use new skills the program directors will go on doing things which have not proved useful, such as attractive dazzling new programs, methods and hardware for communicating information but no change will occur in the behavior of the participant.

One method that is beginning to be built into continuing competence of the physician is periodic recertification.[2] No specialty board has adopted a program for actually getting it done but they are all pursuing the idea. Although they recognize the enormous problems involved. The reason, of course, when they are pursuing it is that being declared competent now does not guarantee competence in the future. Competence has always been a perishable commodity. New knowledge of value in maintaining health and managing disease is being created more and more rapidly. It is estimated that the half-life of knowledge now is less than ten years.

As the years go by and science advances the lessons of medical school and formal graduate training grow less and less useful. Everything fades with time. This is especially noted by the American Board of Internal Medicine in the new scores on the written examination as they progressively fall over a period of years as unsuccessful candidates repeat their efforts to pass. There are others who show great improvement in their scores whose failure has stimulated serious preparation for another trial.[2]

The demands of new knowledge, the reality of human forgetfulness, the demonstrated benefits of review and the Boards wish that its certificates should really mean what they say, have all prompted a move towards recertification. However, it must be born in mind that many problems need to be solved in the process. The first one is how will recertification be earned. If it is an examination, what should the examination cover, and how often should it be required. If allowing credits for attendance at educational and scientific meetings will be one of the elements, then what meetings and how much credit. Since the Board itself is not in the business of education, who will make the facilities available. Although we are moving in the direction of recertification, the procedure must be feasable and we must help develop educational programs which will make it easy for the conscientious physician to meet the requirements.

Brown and Uhl[3] address themselves to the problem of how to improve patient care for it is this area in medicine that continuing education is all about. They consider first a method of identification of specific deficiences in patient care in the hospital setting combined with programs for correction. One way to assist in this area is establishing a method for utilizing specialists to assist in a patient care problem. Focusing on the patient and the learner provides a rational method to estimate success of the program. The final measure of success must be that the patients needs are met.

Most adults, and certainly mature professionals, learn most efficiently and effectively in a problem solving situation. Such situations are seldom provided. In fact, until recently, learning experiences in medical education have been designed to achieve information transfer only. The implication here is that patient care deficits derive from lack of physician learner knowledge. This implication is seldom tested, just as most other assumptions concerning medical education are not tested. Right now we have no real increase of knowledge, regarding deficits, skill defiicits, whether intellectual or psychomotor, or the need for attitudinal changes.

In the standard approach, principles of learning are not considered. There is no active participation, usually no feedback, content is irrelevant to the practices of the intended learner, incentives are likely to be external, whereas powerfully motivating intrinsic incentives that relate the task directly to a goal are needed. The way it is now a lecture is given, but diagnosis of patient care need seldom precedes educational therapy. What really must be measured is success in patient management, the outcome of the physicians effort in diagnosis, prognosis and treatment of his patient. In other words we must start with patient care evaluation, go on to learner evaluation by examination, then program or course evaluation and finally institutional evaluation.—L.H.N.

References

1. Carmichael, H. T., Self-Assessment Tests, JAMA 213, 1656, September 7, 1970.
2. Hickam, J. B., Periodic Recertification Ibid 1657.
3. Brown, C. R. J., Uhl, H. S., Mandatory Continuing Education Ibid 1660.

Treatment of Hypertensive Crisis

Rapid lowering of the diastolic blood pressure is often life-saving in patients in hypertensive crisis or in the malignant phase of essential hypertension. In both conditions, the diastolic pressure is usually above 140 mm Hg, and pulmonary edema or hypertensive encephalopathy—headache, retinopathy, convulsions, and stupor or coma—may be present. Hypertensive crisis occurs in patients with severe renal parenchymal disease, pheochromocytoma, collagen disease, or eclampsia, and in patients who take sympathomimetic drugs or foods rich in tyramine (sharp cheeses, broad beans, meat extracts, chianti wine) while they are being treated with monoamine oxidase (MAO) inhibiting drugs such as pargyline (Eutonyl) and tranylcypromine (Parnate).

CHOICE OF DRUGS—The objective of therapy is the reduction of diastolic pressure to about 110 mm Hg as rapidly as is possible without excessive risk of cerebrovascular or myocardial ischemia or renal shutdown. When renal parenchymal disease is the primary cause of a hypertensive crisis, it is essential to titrate drug dosage against blood pressure and renal function (measured by urinary output and blood urea nitrogen [BUN] or creatinine clearance). When severe renal disease causes irreversible anuria, surgical removal of the kidneys may be necessary, followed by kidney transplantation or dialysis. In surgery for pheochromocytoma, phenoxybenzamine (Dibenzyline) and phentolamine (Regitine), alpha-adrenergic blocking agents, are generally used to control hypertensive crisis.

With other hypertensive crises, if there is stupor, coma, convulsions, impending blindness, or evidence of cerebral or subarachnoid hemorrhage, a rapid-acting drug should be administered intravenously; one of the most effective is trimethaphan camsylate (Arfonad), a sympatholoytic drug. It has an immediate hypotensive action but since it acts for only about 15 minutes, continuous intravenous infusion, with frequent monitoring of the blood pressure, is necessary. A few Medical Letter consultants use pentolinium (Ansolysen) when rapid lowering of pressure is needed. Intramuscular administration of 2.5 to 10 mg lowers the blood pressure in about 10 to 30 minutes with the effect lasting four to eight hours. Parenteral magnesium sulfate has been used as a hypotensive agent, especially in eclampsia, but the unpredictable fall in blood pressure, respiratory depression, and frequent heart block have discouraged wide use.

Some investigators recommend sodium nitroprusside, but it is not available commercially and a solution must be prepared by the hospital pharmacy; 60 mg of the drug is added to a liter of dextrose solution and given by intravenous infusion at a rate of 10 to 30 drops per minute. It acts rapidly, and its effects last about 15 minutes after the infusion is discontinued. Sodium nitroprusside must be stored in brown bottles. When it is used continuously, the infusion bottle must be changed for a fresh solution every 12 hours.

Parenteral hydralazine hydrochloride (Apresoline) is used by several Medical Letter consultants. It acts in about 15 minutes, and its effects last from two to six hours. Because of the cardiac stimulating effect of hydralazine, it is not recommended for patients with coronary disease. A non-diuretic benzothiadiazine drug, diazoxide (Hyperstat-Schering), lowers blood pressure almost immediately, and some investigators are enthusiastic about its effectiveness. It is available only for investigational use in the United States, however.

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FROM THE EXECUTIVE DIRECTOR'S OFFICE

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SUMMARY OF ACTIONS COUNCIL MEETING

Thursday, October 29, 1970

I. Attendance

Present in addition to the Chairman, Dr. S. J. Martin, were: Drs. Granoff, Weber, Jr., Grendon, Burnham, Abbot, Dean, Fabro, Rem, Cramer, Ragland, Jr., Harwood, Pelz, Palomba, Roch, Nemoitin, Van Syckle, Johnson, Freedman, Root, Jr., and vonGlahn.

Also present were: Mrs. Lindquist, Mr. Sullivan, Mr. Tomat, Dr. Hess (Welfare Medical Director), Mr. Gordon (HCMA), Mr. Olson (FCMA) and Dr. Richards.

Absent were: Drs. Edson, Brandon, Wilson, Jr., Friedberg, Harkins, Gorin, Purnell and Klare.

II. Routine Business

Approval of Minutes

As printed and distributed, it was VOTED to approve the minutes of the meeting of September 16, 1970.

Life Memberships

It was VOTED to approve applications for Life Membership submitted by the following eligible Active Members:

Wesley F. Fitzpatrick, 85 East Avenue, Norwalk (FCMA)—1/1/71

Aaron Greenberg, 226 Main Street, Old Saybrook (MCMA)—1/1/71

John E. McNerney, 65 Prospect Street, Stamford (FCMA)—1/1/71

Lloyd W. Minor, 195 South Main Street, Middletown (MCMA)—1/1/71

Thomas F. Murphy, 850 Farmington Avenue, West Hartford (HCMA)—1/1/71

Anthony M. Pernetti, Conn. State Department of Health, 10 Clinton Street, Hartford (MCMA)—1/1/71

Otis B. Schreuder, South Road, Marlborough (HCMA)—1/1/71

Resignations, Appointments, Etc.

(a) *Committee on Accident Prevention:* It was VOTED to accept the resignation of Sherwin B. Nuland, New Haven, as a member of this Committee.

(b) *Connecticut Hospital Planning Commission:* It was VOTED to recommend for nomination to membership of the CHPC, for three-year terms, the following two incumbents:

David A. Grendon, Sharon
E. Tremain Bradley, Norwalk

(c) *CHA Council on Continuing Health Care:* It was VOTED to nominate, for possible appointment to this new council of the Connecticut Hospital Association, the following CSMS members:

Edward S. Scherr, Branford
Michael J. Kelleher, Bridgeport
William J. Murray, Jr., New London

Date of Next Meeting

No Council meeting is planned during November. The Chairman will select an appropriate date (a Wednesday) for the December meeting.

III. Old, New and Special Business

Election of Student Members

It was VOTED to elect to Student Membership 32 Connecticut residents who are attending medical schools in the United States. A list of those elected will be published in an early issue of the Journal.

Report of the Fiscal Advisory Committee

It was VOTED to act on a report filed by the FAC as follows:

Policy re Funding of "Social Hours": To approve the recommendation of the FAC that, in general, it be the policy of the Society that the underwriting of costs for social functions be limited to those incurred for food *only*, and that charges for libations (liquor, beer, etc.) be met by function participants on a "Dutch treat" basis. This policy is intended to apply primarily to regular, recurring internal functions (such as committee meetings, etc.). It has been observed by the Council for more than 20 years.

The 1971 Budget

It was VOTED to approve a budget for fiscal 1971, as prepared by the Budget Committee, and to set the membership dues for 1971 at $70. It was further VOTED to transmit the budget and the proposed dues structure to the House of Delegates on November 19, 1970, with the Council's recommendation that both be approved by the House.

Report—Committee on Investment of Funds

Having been apprised of the Committee's opinion that the Society's present investment portfolio is overly-conservative, an opinion said to be concurred with by the CSMS Investment Counsellor, the Council VOTED to approve the following policy statement with regard to the investment of funds:

> "The policy governing management of the general funds is hereby changed from that of 7/5/62 to embrace a new philosophy as follows: That the general funds shall be invested in such manner as to provide maximum capital growth and income consistent with safety in preserving capital. Enough funds shall be in liquid form to cover at least one month's budgeted expenditures".

Connecticut Medical Service, Inc.

Responding to a letter received from the President of CMS, concerning exploration of the possibility of CSMS and CMS resuming some sort of corporate relationship and the possible terms and conditions thereof, it was VOTED to advise Mr. Betts that the component County Medical Associations always have been, and remain, autonomous with respect to making nominations for membership on the CMS Medical Advisory Committee, and that, having no official relationship with CMS, the Society is not in a position to recommend to the component Associations that they make any change in this regard. It was further VOTED to advise Mr. Betts of the Council's interest and willingness to meet with representatives of the CMS Board of Trustees to discuss possible ways and means of bringing the two organizations closer together. Pursuant to the latter action, it was further VOTED to authorize the President, Dr. Granoff, and the members of the present Liaison Committee with CMS (Drs. Gardner, Martin, Weber and Grendon) to act as an ad hoc committee to initiate such discussions with representatives of the CMS Board of Trustees for the purpose stipulated, and to report to the Council its findings and recommendations.

Confidentiality and Informed Consent— CRMP CUPISS Program

By invitation, the Council was joined by representatives of CRMP (Dr. Williams and Mr. Mills) and by Marvin Garrell, Fairfield, a CSMS designate serving on the CUPISS Technical Advisory Committee, to pursue further the Council's unanswered questions concerning the provisions that are made in CUPISS to protect the rights of patients, by ethical and legal standards, with respect to confidentiality of their medical records and informed consent to feed their data into CUPISS computer systems. It appears that, as of now, only the first two "in-put" phases of CUPISS are under development, and that the "out-put" (retrieval) phase will not be developed to the point of operation until a much later date. The Council was informed that although the legal aspects of confidentiality are presently under study by attorneys engaged by CUPISS, the responsibility for observing confidentiality currently rests with participating hospitals; that until the retrieval phase is made operational, CUPISS has little if any value to practitioners in the care of patients; and that, after January 1, 1971, CUPISS must be funded by private agencies (instead of with Federal tax dollars).

Following extended discussion of the subject, the Council members indicated (by show of hands) that the responses made to their questions by the participating guests, and the explanations of CUPISS procedure given by same, had not served to allay their basic concerns and objections concerning the "confidentiality" and "informed consent" aspects of the program. It was then VOTED to notify the CRMP Advisory Board that, despite the responses and explanations received from the CRMP representatives, the Council still contends that confidentiality and informed consent, by legal standards, have not been adequately provided for in the CUPISS operation. It was further VOTED to apprise the hospitals of the state, the Connecticut Hospital Association and Connecticut Blue Cross of the Council's continuing objections in this regard.

CSMS Endorsement of Research Project

Having received additional information on a proposed research project to study the long term effects of oral contraceptives, and a recommendation for endorsement from the Executive Committee of the Cancer Coordinating Committee, the Council VOTED to reconsider its action (disapproval) of September 16, 1970. The Council members were then joined by Drs. Mayer, Acheson and White, of the Yale School of Epidemiology and Public Health, who elaborated on the protocol of the project and responded to questions concerning same. Following an adequate period of discussion, it was VOTED to endorse the project and to furnish Eugene S. Mayer, M.D., Postdoctoral Fellow, with the following letter of introduction:

> "TO WHOM IT MAY CONCERN:
>
> The Council of the Connecticut State Medical Society has reviewed the proposal of the Chronic Disease Epidemiology Section of the Yale University School of Medicine for a survey of the long term effects of oral contraceptives. The Council recognizes the need for such an investigation and endorses the approach to be taken in the proposed Yale study. The Council urges all members of the Connecticut State Medical Society, who are so requested by the study's investigators, to cooperate in this survey."

Report—Evaluation of "Congressional Contact" Program

It was VOTED to accept, as presented, an evaluation report on the "Congressional contact" visits to Washington, D.C., which have been made annually since 1968. The report was submitted, at the Council's request, by the Committee on National Legislation. In brief, the report covered the areas of: Composition of delegation; size of delegation; time of visit; and general format for itinerary and schedule.

Report—AMA Regional Conference on Peer Review

It was VOTED to accept as information a report on the proceedings of this Conference (Boston, 10/3-4/70) which was filed jointly by Kurt Pelz, Sidney L. Cramer and William R. Richards, who attended as representatives of the Society. The report concluded with a series of recommendations which were acted upon as follows:

(1) It was VOTED to reaffirm the CSMS policy that peer review of physicians services should be made only by physicians, whether such review concerns charges, utilization or quality.

(2) It was VOTED to appoint Morris A. Granoff (Chairman), Kurt Pelz and Sidney L. Cramer as an ad hoc committee, and to both charge and authorize the ad hoc committee to initiate joint discussions on peer review, past, present and future, with representatives (2-3 each) of the Connecticut Hospital Association, Connecticut Blue Cross, Connecticut Medical Service, the Health Insurance Council, Connecticut General (Medicare) and the Welfare Department (Medicaid), with a view to making advance, joint preparations to deal with such conditions, known or anticipated, as a legislated "structured peer review organization" might impose on all parties concerned.

(3) It was VOTED to charge the CSMS Committee on Third Party Payments to make a study of the Hennepin County (Minneapolis, Minnesota) Medical Society type of "health care foundation", and to report its findings to the Council.

Related to these actions, it was further VOTED that the Council establish, at state level, a review committee on fees for, and utilization and quality of physicians' services, for both CSMS members and non-members, the decisions of which shall be applicable. Refinement of this action, including appointment of the committee, appointment of a chairman, sources of committee members, outlining duties and *modus operandi*, etc., will be placed as an item of business on the agenda for the next Council meeting.

Reports—Committee on Public Health

(a) *Resolution on Rho Gam Administration:* It was VOTED to adopt a resolution on this subject, and to refer it to the Committee on Hospitals for appropriate implementation at hospitals, in consultation with the Committee on Public Health and the Committee on Perinatal Morbidity and Mortality.

(b) *Health Education in Public Schools:* It was VOTED to approve the draft of a bill which would require public schools to include health education programs in their curricula on a sequential basis (starting in Kindergarten), covering the essentials of personal health and hygiene, effects of alcohol, nicotine and controlled drugs (instead of narcotics), etc. It being understood that such bill will be sponsored (introduced) by one or more other agencies, it was further VOTED to direct the Committee on State Legislation to take appropriate action in support of said bill.

(c) *Resolution on Office of Health Director:* It was VOTED to adopt a subject resolution which affirmed the position that directors of health, whether on the local, district, regional or state level, should be duly qualified doctors of medicine, and to refer this adopted position to the Committee on State Legislation for appropriate legislative support. It is understood that opposition to bills which would change the present statutory requirement that health directors be M.D.'s is the action called for.

(e) *Resolution on Education Concerning Drug Abuse and the Treatment of Drug Dependency:* It was VOTED to adopt this resolution, in principle, and to encourage the Committee on Public Health to consult and cooperate with the Committee on Mental Health, the Committee on Drug Education (Dr. DeJong) and the Ad Hoc Committee on Drug Counselling (Dr. Pelz) in a joint effort to develop and implement educational programs in the subject areas, both for the profession and for the public.

Connecticut Regional Medical Program

(a) *High Energy Radiation Therapy Services Study:* It was VOTED to receive as information notice that CRMP has approved a plan to study high energy radiation therapy services in Connecticut, submitted by the Connecticiicut Hospital Planning Commission, and has awarded CHPC funds with which to carry out the study. It was further VOTED to direct the Executive Director to participate with staff representatives from some 9-10 other interested agencies in a preliminary evaluation of the proposal in terms of the roles that the participating agencies may be asked to and/or can play. It is assumed that, subsequently, professionals in the subject field will pursue the study to its completion.

(b) *CRMP's "Grand Strategy":* The President, Morris A. Granoff, shared with the members of the Council his concern that CRMP continues to represent that, as part of its "grand strategy", it has an obligation to seek to restructure the present systems for delivering and financing health care services in such manner as CRMP deems "best" for the people of Connecticut. He noted, also, that spokesmen for the national RMP agency are now beginning to make similar representations, and recalled the earlier CRMP statement (in the 1968 Grant Request) to the effect that those representative agencies of health care service providers which did not see eye-to-eye with CRMP on policy and program matters might have to elect to "go it alone". Finally, he reminded the Council members of the section of the RMP enabling legislation which specifically prohibits interference (by RMP activities) with established methods of delivering and financing health care services.

Following the making of these explanatory remarks, Dr. Granoff introduced a resolution which, amended, was adopted by the Council as follows:

RESOLVED: That the Council of CSMS express disapproval of the direction that CRMP activities continue to take; and be it further

RESOLVED: That notice of this action be sent to the Chairman of the CRMP Advisory Board, to the Acting Director of (national) RMP Services, to the Secretary, Undersecretary and Assistant Secretary for Health of HEW, and to the Senators and Representatives in Congress from Connecticut.

It was further VOTED to request Dr. Granoff to elaborate on the word "direction" (in the first "RESOLVED") so as to pinpoint its meaning with regard to CRMP activities.

Recommendations to Hospital Cost Commission

It was brought to the attention of the Council that Mr. Edward S. Karnasiewicz, Executive Director of the HCC, had recently (June 12, 1970) submitted to the Commission a series of recommendations for restructuring and increasing the authority of the Commission so that it could regulate and control most aspects of health care in Connecticut, both private and public, and could exercise its "cost control" function in the area of professional service providers' fees. At present, the Commission's jurisdiction is limited to institutional services (hospital and extended care facilities) when such services are rendered to beneficiaries of medical assistance programs run by the state and for which the state must make payment.

Recognizing that Mr. Karnasiewicz' recommendations are far-reaching in nature, and, if implemented, would have major significance for both institutional and professional providers of health care services, it was VOTED to refer the document and the subject to the Committee on Hospitals with the request that the recommendations be discussed jointly with representatives of the Connecticut Hospital Association (and, perhaps, the Connecticut Extended Care Facility Association) and that a report be made to the Council at the earliest time possible.

Report—Ad Hoc Committee to Study Abortion

The Council was advised that this Ad Hoc Committee (Council-appointed) was in the process of finalizing a report and recommendations which would call for the Society to alter its present position on abortion law "reform", but that it had not proven possible for the Committee to submit said report and recommendations in time for consideration by the Council at this meeting. On this account, it appeared evident that the report could not be transmitted to the House of Delegates as a "report of the Council", with recommendations, as previously-established protocol called for. After considerable discussion, including the expression of a consensus of opinion that a special meeting of the Council to receive the report was not practical, it was VOTED to submit the report of the Ad Hoc Committee, when received, *directly* to the House of Delegates as an item of business for consideration and action.

N.B.: *The foregoing is a summary of the proceedings and action of the Council on October 29, 1970. Detailed minutes of the meeting are on file at 160 St. Ronan Street, New Haven, for perusal by any interested member of the Society.*

Placement Wanted

DERMATOLOGIST—30 years of age, Eligible with National Boards wishes solo type practice in a medium or small size community in Connecticut. (Preferably not too far from a large city). Presently in practice.

EMERGENCY ROOM—28 years of age, National Boards, wishes institutional type practice in a large or medium size community in Connecticut. Contact: Robert J. Riggen, M.D., 155 Poopoo Place, Kailua, Hawaii 96734.

GENERAL PRACTICE—32 years of age, with National Boards, wishes group type practice in Connecticut. Available in November when military obligation completed. Contact: Lee M. Dippery, Major, MC, M.D., H.Q. 6/10 Field Artillery, New York APO 09139.

GENERAL PRACTICE—61 years of age, wishes solo, group, institutional or industrial type practice in Connecticut. Presently in practice. Would prefer a position with a pharmacy firm or as a plant physician. Contact: Erich Russow, M.D., 71-18-69 Place, Glendale, New York 11227.

INTERNIST—38 years of age, Eligible wishes group or industrial type practice in Connecticut.

Will consider any position. Connecticut license. Presently available. Contact: Declan Foley, M.D., 76 North Pearl Street, Meriden, Connecticut 06450.

INTERNAL MEDICINE—44 years of age, Eligible, wishes industrial type practice in Connecticut. Presently in practice. Interested in a position in medical electronics, research, development, testing, etc. Available immediately. Contact: Keith Lusted, M.D., 939 Oak Street, S.E., Salem, Oregon 97301.

INTERNIST—34 years of age, Eligible wishes solo, associate or group type practice in Connecticut. Connecticut license.

INTERNIST—32 years of age, qualified (and Eligible), with National Boards and Connecticut License, two years experience in cardiology wishes to join group or associate type practice in southern Connecticut. Military obligation completed.

INTERNIST—36 years of age, Eligible, wishes group or institutional type practice in a medium or small size community in Connecticut. Presently in practice. Prefer hospital-based group or full-time.

INTERNIST/CARDIOLOGY—30 years of age, Eligible with National Boards wishes associate type practice in a medium size community in Connecticut. Would like to associate with 1-3 other Internists. Military obligation completed.

INTERNIST—45 years of age, Certified, wishes group, institutional or industrial type practice in Connecticut. Available immediately. Contact: John G. Swadey, M.D., 132 Phillips Road, Pembroke, Mass. 02359.

INTERNIST—33 years of age, Eligible with National Boards, wishes group, associate or institutional type practice in a large or medium size community in Connecticut.

NEUROSURGERY—35 years of age, Certified, wishes group, institutional or academic type practice in a large or medium size community in Connecticut.

OBSTETRICS & GYNECOLOGY—34 years of age, Eligible, wishes group or associate type practice in a medium size community in Connecticut. Military obligation completed in January 1971.

OPHTHALMOLOGY—31 years of age, National Boards, wishes solo type practice in a medium size community in Connecticut. Military obligation completed. Contact: Stephen H. Franklin, M.D., 555 E. William Street, Ann Arbor, Michigan 48108.

OPHTHALMOLOGY—29 years of age, Eligible with National Boards, wishes solo, group or associate type practice in Connecticut. Military obligation completed.

OPHTHALMOLOGIST—31 years of age, Eligible wishes to practice in Connecticut. Connecticut License. Extensive subspecialty training.

PATHOLOGIST—39 years of age, Certified with National Boards, wishes associate type practice in a medium size community in Connecticut. Connecticut license. Desires position as chief Pathologist or laboratory director. Contact: Sanford H. Edberg, M.D., Lee Hospital, 320 Main Street, Johnstown, Pennsylvania 15901.

PATHOLOGIST—35 years of age, with National Boards, wishes group, associate or institutional type practice in Connecticut.

PATHOLOGIST/ANATOMIC—48 years of age, Certified, wishes institutional type practice in Connecticut. Presently in practice. Would prefer an academic center, since interested in routine work, teaching and research. Available early 1971.

PEDIATRICIAN—29 years of age, certified with National Boards, wishes group or associate type practice in a large or medium size community in Connecticut. Available shortly. Contact: Philip H. Friedman, M.D., 287 Dickman Drive, Loring AFB, Maine 04750.

PEDIATRICIAN—47 years of age, Certified, wishes group or associate type practice in a large or medium size community in Connecticut. Presently in practice.

SURGEON—33 years of age, wishes group or associate type practice in Connecticut. Certified with National Boards. Available immediately.

SURGERY—28 years of age, Eligible, wishes solo, group or associate type practice in Connecticut.

SURGERY—42 years of age, Eligible, wishes group or associate type practice in Connecticut. Wishes to practice surgery with no general practice in an association or group. Available immediately. Contact: A. Sergie, M.D., 2035 Pine Street, Phila. Pa. 19104.

ANYONE INTERESTED IN THE ABOVE IS ASKED TO CONTACT THE PHYSICIANS PLACEMENT SERVICE, 160 ST. RONAN ST., NEW HAVEN, CONNECTICUT 06511.

Placement Opportunities

ANESTHESIOLOGIST—position available for associate to board-certified anesthesiologist in an attractive progressive general hospital. Excellent staff. Generous remuneration. Minimum amount of call with maximum vacation time. Write or call: Dr. Marvin Albert, World War II Veterans' Memorial Hospital, Paddock Avenue, Meriden, Connecticut 06450. Telephone 203-237-5531.

DISTRICT HEALTH DIRECTOR for Westport/Weston, Connecticut. Requires M.D., degree in Public Health or equivalent experience, and eligibility for Connecticut license. Salary range $22,000 to $26,000 depending on qualifications. Population served, 35,000. Excellent schools cultural and recreational opportunities. Position available October, 1970. Send resume to Clifford W. Mills, M.D., Chairman, Aspetuck Valley Health District Board, 180 Bayberry Lane, Westport, Connecticut 06880.

OPPORTUNITY FOR INTERNIST OR GENERAL PRACTITIONER for association with General Practitioner. A good family practice in urban community in Connecticut. No Ob or major surgery. Part-time University position if desired.

GENERAL PRACTITIONER.—The town of East Lyme is in need for two other general practitioners. Year round population of 11,000; a summer population of at least 15,000. A lovely community on the shore of Long Island Sound, is close to the Submarine Base and the Coast Guard Academy. There is an instant practice for a General Practitioner, and a fully equipped office and laboratory available for rent. 50 miles from Hartford, and 10 miles from New London. The Lawrence and Memorial Hospital in New London is a 327 bed modern hospital, fully staffed and equipped, with nursing school and intensive care unit. A 40 bed addition is underway, with a new X-ray department. Contact: First Selectman, Town of East Lyme, P.O. Drawer 519, Niantic, Connecticut 06357. (203-739-6246).

GENERAL PRACTITIONER—presently hospitalized, 16 years lucrative practice, in search of immediate coverage, association or partnership. Rented office fully equipped with three examining rooms, X-ray equipment, dark room. One senior nurse's aide and one receptionist immediately available. Centrally located town to 6,500, near large cities. To hospitals, with 24 hour emergency coverage nearby. For further information contact: Mrs. Sophy M. Graves (office nurse), Parum Road, Colchester, Connecticut. 537-2836.

OBSTETRICS & GYNECOLOGY—Board eligible or rated, to immediately take over 20 year successful solo practice. Coastal Fairfield County. Token investment. Will introduce if available. Connecticut license required. Must be available soon. Incumbent leaving area permanently. Lease available.

OBSTETRICS & GYNECOLOGY—Excellent opportunity. Board eligible or certified associate needed. Early partnership. For further information contact: William P. Canty, M.D., 110 Church Street, Putnam, Connecticut 06260.

OFFICE/HOME combination for sale. Connecticut shoreline. Seven room office fully equipped including X-ray, fluoroscope, EKG etc. Dark room and laboratory. Excellent opportunity for immediate income from active, lucrative practice. Close proximity to Yale New Haven Medical Center and Middlesex Memorial Hospital, Middletown, Connecticut. Physician recently deceased. For details write to: P.O. Box 222, Clinton, Connecticut 06413.

PATHOLOGIST—Board certified AP-CP with 3-5 years experience, to associate with director of modern laboratory in accredited voluntary hospital nearing completion of expansion to 400 beds. Active teaching program for interns and residents; medical school affiliation. Write: Dr. I. Rothstein, Mount Sinai Hospital, Hartford, Connecticut 06112.

PEDIATRICIANS—Two board certified Pediatricians seek dynamic young associate to join rapidly expanding practice and medical community for the general practice of Pediatrics. Excellent salary to partnership. Equal time off. No investment necessary. For further information contact: Thomas J. McGrath, M.D., 108 New London Turnpike, Norwich, Connecticut 06360. (203) 889-3835.

PEDIATRICIANS—opportunity in area of 75,000 for hospital-based private practice or community-based private practice. Modern 250 bed, Yale affiliated, general hospital in Southern Connecticut suburban community. Excellent diagnostic services available. Attractive living conditions. Reply to: Administrator. Griffin Hospital, Derby, Connecticut 06418.

PEDIATRICIAN to join two board certified Pediatricians with growing, well developed practice. New Office designed for three men. Excellent community and hospitals. Equal time off. Salary plus bonus first year; then partnership. For further information contact: Edward P. Wallace, M.D., 285 Broad Street, Meriden, Connecticut 06450, 203-238-1257.

PHYSICIANS—Five room office fully equipped with X-ray and laboratory. Located in beautiful southern Connecticut shoreline area. Six blocks from Community Hospital, which is expanding. The hospital is the only one within 45 mile radius. Community over 40,000 people which consists of several small towns with population 3,000 to 14,000 each.

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William D. McCurry, M.D., 109 Broad Street, Middletown, Conn. 06457.

Treatment of Obsessive-compulsive Neurosis with Haloperidol

(*Can. Med. Assoc. Jr.* 103, 167, July 18, 1970). The author describes 2 cases of obsessive-compulsive neurosis. One a farmer, age 57, agitated and depressed who constantly worried about minor problems of compulsive habits. Nothing worked including electroconvulsive therapy, but haloperidol 5 mg. per day relieved him. He developed some extrapyramidal symptoms which were relieved by ethopropazine HCl, 50 mg. t.i.d. The relief, however, was not sufficient to permit him to return to work.

The second patient, aged 45, had compulsive ritualistic acts that prevented him from functioning over a period of 10 years. Five mg. haloperidol not only stopped his ritualistic behavior but also his mental compulsions to do so. He was able to return to work.

It appears that haloperidol is the most valuable drug available to relieve the suffering of those unfortunate enough to have developed a neurosis which has a poorer prognosis and is more handicapping than most psychoses.—L.H.N.

In Memoriam

DeCristoforo, Ralph, Tufts Medical School, 1937. Dr. DeCristoforo was a general surgeon in the Waterbury area since 1937. He was medical advisor to Waterbury Draft Board II and served as assisting attending surgeon at St. Mary's Hospital. Dr. DeCristoforo did post graduate work at the Surgical Anatomy Polyclinic in New York and was a member of the New Haven County Medical Association, the Connecticut State Medical Society, the American Medical Association, the American Academy of General Practitioners, and the American Society of Abdominal Surgeons. He died October 19, 1970, at the age of 60.

Hinckley, Elizabeth Brennan, College P & S, Columbia University, 1936. Dr. Hinckley was retired and residing in Guilford at the time of her death. She was a member of the American Academy of Pediatrics, and attending pediatrician at St. Luke's Hospital in New York and was also a member of the Connecticut State Medical Society. Dr. Hinckley died October 29, 1970, at the age of 67.

Jackson, Allen F., Howard University, 1922. Dr. Jackson was a general practitioner in the Hartford area since 1923. He was attending physician at St. Francis and McCook Hospitals. Dr. Jackson was a member of the Hartford County Medical Association, the Connecticut State Medical Society and the American Medical Association. Dr. Jackson died October 9, 1970, at the age of 73.

Marranzini, Samuel, N.Y.U. and Bellevue Medical School, 1928. Dr. Marranzini was an eye, ear, nose and throat specialist in the Hartford area since 1931. He was on the staff of St. Francis Hospital, and was a member of the Hartford County Medical Society, the Connecticut State Medical Society and the American Medical Association. Dr. Marranzini died October 6, 1970, at the age of 70.

Pomeroy, William Henry, University of Maryland, 1943. Dr. Pomeroy was a general practitioner in the Hartford area since 1947. He was on the staff of Hartford Hospital and was a member of the Hartford County Medical Association, the Connecticut State Medical Society and the American Medical Association. Dr. Pomeroy died October 5, 1970, at the age of 55.

Adverse Effects of LSD: A Current Perspective

David J. Greenblatt, M.D. and Richard I. Shader, M.D.

Abstract

Certain adverse neuropsychiatric sequelae are known to be associated with the use of LSD. These include the dangers of acute intoxication, as well as the possibility of prolonged or recurrent reaction. While repeated and multiple drug use as well as emotional instability are thought to predispose to such adverse reactions, neither the true incidence nor the long-term significance of such untoward reactions are understood at the present time.

Recent reports have implicated LSD in cytogenetic damage, both in animals and in man, with possible teratogenic or carcinogenic results. A critical survey reveals that these reports do not provide sufficient evidence either to confirm or rule out an adverse cytogenetic effect of LSD.

A Current Perspective

The increasing prevalence of the illicit use of hallucinogenic drugs by American youth has stimulated much concern regarding the adverse effects of these agents. A large part of the controversy has centered around lysergic acid diethylamide (LSD), one of the first of a large number of hallucinogenic drugs which are currently in wide use. Unfortunately, much of the rational discussion regarding the dangers of LSD has been obscured by highly emotional rhetoric on both sides, as well as by an intolerant moralistic and legalistic attitude by many of the "adult" generation, so that it may be difficult even for physicians to obtain a realistic overview of the dangers associated with the use of LSD and related drugs. The purpose of this article is to begin to provide such an overview.

Much literature has been devoted to the psychopharmacology of LSD as well as to the nature and implications of the LSD experience.[1-6] Most familiar of the adverse effects of this drug are certain neuropsychiatric sequelae which have been observed and reported for more than a decade. A separate category of untoward effect has been suggested by a number of confusing and contradictory reports appearing since 1967 which discuss the possible role of LSD in cytogenetic damage.[7, 8] These recent reports have redoubled the controversy over the dangers of LSD, and only reemphasize the necessity for rational interpretation of the available information.

Neuropsychiatric Effects

The category of neuropsychiatric complications of LSD has been the subject of a number of excellent review articles.[9-15] A helpful subdivision of this category is as follows:

Dangers Associated with Acute Intoxication

While the intoxicated state induced by LSD is not strictly a "model psychosis", delusions, hallucinations, and confused ideation are common manifestations.[16] Grandiose delusions of invulnerability may result in self-destructive acts, while paranoid delusions may lead to overwhelming fear, violence, and even homocide. Depression is also common, and may be so intense as to result in suicidal attempts. LSD users who experience "bad trips" in which hallucinations are unpleasant or the experience in general does not conform to their expectations may become extremely anxious, occasionally to the point of terror and panic such that hospitalization and sedating medication is necessary.[17]

Prolonged Reactions

Pharmacologic studies have demonstrated the half-life of LSD in humans to be in the range of three hours.[18] Trace amounts are detectable in the

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plasma eight hours after ingestion, and the drug is essentially completely eliminated after twelve to twenty-four hours. In general a similar time course of subjective sensations is noted, after an oral dose of LSD, with symptoms being maximal a few hours after ingestion, then subsiding and disappearing in twelve to twenty-four hours. In some subjects, however, symptoms may persist long after the drug has been eliminated; rarely, the "intoxication" can be permanent. These prolonged adverse reactions may be a persistence of depression, anxiety, terror, and fear of becoming insane which were experienced during the acute drug experience, or else may be a persistence of hallucinations, delusions, paranoid thinking, and other psychotic manifestations.

Recurrent Reactions

In some subjects the symptoms characteristic of acute LSD intoxication may recur spontaneously, unassociated with the taking of the drug. These so-called "free trips" or "flashbacks"[19] are a poorly understood phenomenon. It is possible that a period of great mental stress may "trigger" such a spontaneous recurrence, similar to the stress-precipitated recall of horrifying war experiences in soldiers with "war neuroses." Smart and Bateman[7] further have noted that LSD "flashbacks" are most often reported in patients who have ingested LSD numerous times (up to 300), speculating that a cumulative toxicity of some kind may be involved. Also reported have been spontaneous recurrences following therapeutic administration of another psychotropic drug such as chlorpromazine.[20]

The untoward neuropsychiatric complications of LSD as described above are recognized as being very real dangers associated with the use of this drug. It must be emphasized, however, that the incidence of these complications with respect to the total LSD-taking population is unknown at the present time. Statistical reports are few in number, and results are generally equivocal because of obvious but usually unavoidable errors in methodology.[21] Nevertheless, it is the impression of most reviewers that a *large majority* of LSD users experience no adverse effects whatsoever. The present authors know of many individuals, including physicians, who have repeatedly used LSD without untoward effects. This is not to belittle the magnitude of the problem, since even a small incidence of complications is very significant if the number of users is very large. Cohen[22] has estimated an incidence rate of prolonged psychotic reactions to LSD in the range of 0.8-1.8 per 1000 LSD users, an estimate which is probably too small. Even at this incidence, such reactions could be expected to number 8,000 to 18,000 if the total number of users is ten million.

Regardless of the actual incidence of LSD complications, it is thought that the risk of untoward reactions is greater in those who use the drug repeatedly and in unsupervised settings, and in those who simultaneously ingest other psychoactive agents. Also at greater risk are those who are emotionally unstable or who have a previous history of psychiatric disturbance. Some authors explain the prolonged psychotic reactions to LSD as an unmasking by the drug of mental illness in an individual who already was so predisposed, rather than as a manifestation of a permanent neurological or psychiatric effect of the drug itself. This subject is currently a matter of dispute.[23]

The setting in which LSD is taken is thought to be an important determinant of the nature of the subjective drug experience. Subjects who take LSD alone or in poorly supervised or uncongenial surroundings are more likely to experience anxiety or panic reactions than those who use LSD in a therapeutic setting or with sympathetic, understanding peers. In the past, acute panic reactions were thought to require sedative medication and hospital supervision for treatment. It is now recognized that the large majority of such reactions respond well to sympathy and reassurance by physician or peers, and do not require hospitalization or sedation. Panic often can be alleviated simply by reassuring the patient that the intoxicated state is only temporary and is due entirely to the drug, and that he is not "losing his mind." Prevention of panic reactions by proper adjustment of setting, however, remains the most powerful deterrent.

Cytogenetic Effects

Apprehension regarding chemically-induced teratogenic and carcinogenic effects is widespread among the lay public and the medical profession alike. The large number of tragic deaths and deformities resulting from cigarette smoking or thalidomide, for example, serve as a constant reminder that drugs and other exogenous agents may indeed have such effects. It is little wonder that recent reports of chromosomal damage associated with LSD, with implications and speculation that such damage may result in malignancy, malformed fetuses, or inheritable genetic alterations, have generated much concern and discussion. Perhaps it is equally tragic that much of the research upon which the speculations are based is inconclusive and of poor quality, but has nevertheless served to increase the moral and legal resistance to further useful research which may provide a reasonable answer to the question of LSD-induced cytogenetic damage in humans.[24]

Drosophila

There are four published reports of studies involving LSD and the fruit fly, *Drosophila melanogaster*. In these studies, LSD is administered to male flies either orally or intraperitoneally. The males are then mated with normal females, and the incidence of lethal mutations in subsequent generations is determined. Two studies[25, 26] showed no difference in lethal mutation rate between LSD and control. Two others[27, 28] showed LSD to be mutogenic only after huge doses, in the range of 400-1250 mg/kg, which in one report produced partial sterilization in addition. A typical human dose is 0.001-0.003 mg/kg. Grace, *et al*[26] also studied premeiotic, meiotic, and postmeiotic sperm in male flies treated with 0.2-100 mg/kg of LSD, and found no visible chromosomal abnormalities.

These studies demonstrate that ordinary doses of LSD do not produce lethal mutations in *Drosophila*. These findings are of interest, but are of little value either in predicting or ruling out a possible teratogenic or mutagenic effect of LSD in higher animals or humans.

Meiotic Chromosomes in Mice

Studies involving the effect of LSD on meiotic chromosomes in testicular tissue of male mice have produced inconsistent results. Skakkebaek, *et al*[29] examined meiotic cells of six mice receiving at least 1 mg/kg of LSD, two to ten days after the last dose, and found 4% of cells to have chromosomal abnormalities as compared to 0.7% of cells in six untreated mice. Cohen and Mukherjee[30] administered 25 μg/kg to thirteen mice whose meiotic chromosomes were examined 1 to 21 days after the last dose. 3.4% of cells were abnormal in the LSD-treated animals examined two to seven days after the last treatment, as compared to 0.3% of cells in control animals. The percentage of abnormal cells declined as the time since LSD treatment increased past one week. Animals examined three weeks after the last dose showed an incidence of abnormal meioses very close to that of the controls.

Jagiello and Polani,[31] on the other hand, found no increase in abnormal meioses in 24 mice treated with 17-170 μg/kg of LSD administered subcutaneously daily for 31 days, nor in six mice receiving a single dose of 1 mg/kg. These investigators also studied the ova of female mice treated with LSD both in *vivo* and *in vitro*, and found no increase in abnormalities. The reason why this study failed to replicate the findings of the two other reports is not obvious.

Again it must be emphasized that the applicability of these results to humans is dubious. The doses used in those studies with positive findings (25-1000 μg/kg, repeatedly) are very large compared to a usual human dose of 1-3 μg/kg. Moreover there was no investigation of the question of whether the observed chromosome abnormalities were of any significance in terms of the production of abnormal offspring.

Pregnancy in Animals

Studies of the teratogenic effect of LSD in pregnant rats, mice, hamsters, and rabbits have produced remarkably inconsistent results. Geber[32] administered 0.8-240 μg/kg of LSD parenterally to pregnant hamsters on the eighth day of pregnancy, and found 6.6% of subsequent offspring to be deformed as compared with 0% of offspring in control animals. DiPaolo, *et al*,[33] on the other hand, administered 100-3000 μg/kg to hamsters on days 6-8 of pregnancy, and found no teratogenic effect whatsoever. The same authors studied the effect of 17-1000 μg/kg of LSD given to mice on day 7 of pregnancy, and found the results to be dependent on the breeding strain of mice under study. In one strain no abnormal offspring were observed, while in another 19% of offspring were deformed. Auerbach and Rugowski[34] observed 58% of mouse offspring to be deformed after a smaller dose of 3-30 μg/kg given at the same stage of pregnancy.

Studies on rats have demonstrated that the stage of pregnancy during which LSD is administered is an important determinant of the teratogenic effect. Alexander *et al*[35, 36] found that 5-20 μg/kg of LSD on days 1-4 of pregnancy produced 11% abnormal offspring as compared with a 2% deformity rate in controls. LSD given late in pregnancy had no effect. Warkany and Takacs[37] also found no adverse effect of LSD (1.5-300 μg per animal, weights not specified) given after day 4 of pregnancy.

In a single study of New Zealand white rabbits,[38] 20-100 μg/kg of LSD produced no fetal abnormalities when given on days 4-12 of pregnancy, although 100 μg/kg given on days 7-9 produced offspring which were significantly lighter in weight than controls. Kato *et al*[39] report preliminary results of the administration of .125-1.0 mg/kg to four pregnant Rhesus monkeys during the third and fourth months of gestation. Two of the four resulting infants were stillborn and a third died a month after birth. Infants of two non-treated controls were healthy.

In all of these experiments large doses of LSD were administered. Results are inconsistent, and the teratogenicity of LSD seems to depend more upon the particular strain of animal used and the time of administration rather than upon the dose of drug. Nevertheless, there is a suggestion that LSD may be teratogenic under certain conditions.

Human Leukocytes in Vitro

Five sets of data have appeared in the literature describing the cytogenetic effects of LSD upon *in vitro* cultures of human leukocytes (Jarvik and Kato have reported one set of results in three different publications).[40-42] Four of these five groups of data show that cells cultured in media containing LSD have a significantly greater incidence of chromosomal aberrations than cells from a control culture.[40-45] Concentrations of LSD ranged from 0.001 to 10 μg/ml, and the duration of culture before harvest and examination ranged from 4 to 72 hours. Broken or abnormal chromosomes were seen in anywhere from 2.6 to 5.2 percent of cells from control cultures, and in 5 to 33 percent of cells cultured in LSD. The frequency of such chromosomal abnormalities did not seem to depend in an obvious way upon the concentration of LSD or the duration of culture. Only Sturelid and Kihlman[46] failed to find an increased breakage rate after culture with LSD.

Pharmacologic studies in humans have demonstrated that a single dose of 2 μg/kg of LSD results in plasma levels greater than 0.001 μg/ml for eight hours of more.[18] It may then be that the *in vitro* chromosome-damaging potential of LSD may be relevant to humans who ingest this drug. On the other hand, the clinical significance of such chromosome damage to leukocytes, if it occurs *in vivo* as well, is not known. Jarvik and Kato[42] simultaneously studied the *in vitro* effect of aspirin upon leukocytes and found that this agent produces an incidence of chromosomal abnormalities essentially identical with that of LSD. In a discussion of a paper by Judd, *et al*[47] Jarvik points out that a large number of chemical agents, including caffeine, penicillin, and phenobarbital, produce similar chromosome damage *in vitro*. The clinical significance of this damage, if it occurs *in vivo*, is uncertain, and the same can be said for LSD.

In Vivo Studies—Retrospective

There are sixteen studies in which the incidence of chromosome abnormalities in leukocytes of LSD users is compared with that of controls who have not taken LSD. Seven of these studies, involving a total of 83 LSD-takers and 150 controls, show the users of LSD to have a greater incidence of damaged chromosomes than controls,[43, 45, 48-52] nine studies, involving 87 LSD-takers and 77 controls, show no difference.[44, 47, 53-59] The term "leukocyte" is used loosely by most of these authors, and in actuality it is the lymphocyte and not the polymorphonuclear leukocyte which is the cell under study in all cases.[60] This fact is of great importance since the life span of the leukocyte is in the range of two to three weeks,[61] while that of the lymphocyte is approximately eighteen months.[62] Thus an investigation of chromosome damage in a true polymorph would have little value unless peripheral blood were examined within three weeks of the last dose of LSD. Blood samples were drawn *after* this length of time in most of the studies cited above.

Nevertheless the design of nearly all of these experiments is such that the validity of the findings can be seriously questioned. Of greatest concern is the fact that the LSD-taking populations are not at all comparable to the control populations. In many cases the users of LSD are from "hippie" cultures in which the incidence of malnutrition, exposure, viral diseases, and venereal diseases is high,[63] and in which many other hallucinogenic agents and drugs of abuse may be ingested as well. Moreover the LSD taken by these subjects is often of the "street" variety, which is impure and diluted by unknown substances.[64] All of these influences may in themselves cause chromosomal damage and many contribute to the increased incidence of such damage observed in this population.[65] In addition, the incidence of chromosomal aberrations observed in control subjects varies widely between investigators. Some authors have reported that only 0.1% of cells in "non-drug controls" show abnormal chromosomal patterns,[49] while others report a 9% incidence in their "control" group,[51] with some subjects having an incidence as high as 25%. Such wide variations in "baseline" breakage rates makes the significance of drug-induced chromosomal damage difficult to interpret. Finally there are several studies[47-48, 52, 55, 58] in which more than two years had elapsed between the last dose of LSD and the time of chromosome examination, for all or some of the subjects. Since this is considerably longer than the average turnover time of a lymphocyte, these investigations are of dubious value. In two studies,[44, 49] the time between the most recent LSD ingestion and examination of chromosomes is not specified.

Because of these flaws in design, the *in vivo* retrospective studies provide very little useful knowledge as to the cytogenetic effect of LSD in humans.

In Vivo Studies—Prospective

There are three published studies in which the incidence of leukocyte chromosomal damage is determined in a single group of subjects both before and after a dose of LSD. Corey, *et al*[44] studied ten patients who received 200-600 μg of LSD orally, and found no increase in chromosomal damage 24 hours after the single dose. Tjio, et al[86] administered 50-450 μg of LSD to 32 hospitalized neurotic or alcoholic patients, and similarly found no increase in the incidence of cells with abnormal chromosomal patterns. Hungerford, *et al*[67] studied three patients and demonstrated increased damage after an intravenous dose of 200 μg of LSD. They did not test their results for statistical significance because of the small sample size.

The prospective studies are without the flaws in design of the retrospective studies, and thus the results are more meaningful. Two of the three investigations, involving 42 of the total 45 subjects, show that a single dose of LSD does not increase the incidence of chromosomal damage in leukocytes. Again it must be emphasized that the clinical significance of these observations is uncertain.

Human Pregnancy

Reports of the effect of LSD upon human pregnancy add very little useful information as to the possible role of LSD as a teratogen. Berlin and Johnson[68] surveyed some 125 pregnancies in 112 women from a hippie subculture, all of whom were known to have ingested LSD during pregnancy. Approximately 6% of live births from this group had severe congenital anomalies, as compared with an expected frequency of 0.6% in a normal population. Like the retrospective *in vivo* studies, however, this study is poorly controlled, since the population under examination is at extremely high risk for the production of deformed offspring, so that the teratogenic effect of LSD itself cannot be realistically assessed. McGlothlin, *et al*[69] surveyed 148 pregnancies of which both parents had at some time taken LSD. Only a few of the women had taken LSD during pregnancy. These investigators found the ingestion of LSD by the male parent had no effect upon the incidence of spontaneous abortions or congenital defects, nor did LSD ingestion by mothers (usually prior to conception) result in increased numbers of birth deformities. An increase in spontaneous abortions was observed in the LSD-taking mothers. Again, however, the comparability of control and experimental populations with regard to variables other than LSD is not known, so that the significance of this finding is likewise uncertain. A similar criticism may be made of the study of Cohen, *et al*,[70] who found the leukocytes of nine children exposed to LSD in utero to have more chromosomal damage than "control" infants. None of the nine infants were abnormal.

There are three case reports of infants with various congenital deformities of extremities born to mothers who had ingested LSD and other drugs during the first trimester of pregnancy.[71-73] A fourth report[74] describes an infant with documented D trisomy and D/D translocation born to a mother who had taken LSD prior to conception, and other drugs during pregnancy. The infant died of respiratory distress syndrome nine hours after birth. Sato and Pergament[75] describe a mother who ingested LSD prior to conception and on the 43rd and 57th day of pregnancy; the infant was normal and healthy at birth.

While case reports such as these are of interest. they do not establish a causal role of LSD in the production of birth deformities, nor do they provide information as to the incidence of teratogenic effects associated with LSD. It should also be noted that these reports also involve females from "high risk" populations.

Leukemia

Grossbard, *et al*[76] describe the case of a nineteen year old college student who developed acute leukemia four months after the last of fifteen doses of LSD. A "Philadelphia" chromosome, usually characteristic of chronic myelogenous leukemia, was observed in this patient's peripheral leukocytes. This patient had also abused other drugs along with LSD, and in addition had a strongly positive family history for hematologic disease with at least six close relatives having hereditary spherocytosis. Other authors have reported a "Philadelphia"-like chromosome *in vivo* in takers of LSD.

Garson and Robson[77] report a twenty-three year old male who developed acute lymphatic leukemia with no "Philadelphia" chromosome, seven months after the last of many therapeutic doses of LSD. This patient had a strong family history of malignancy, with two female siblings having died before the age of four of malignant disease.

Again such case reports are of interest but fail to establish a carcinogenic property of LSD. As Garson and Robson point out, "the association between the ingestion of lysergide and the occurrence of acute leukemia may be casual rather than causal."

Summary

The risk of certain adverse neuropsychiatric sequelae are known to be a very real danger associated with the use of LSD. However, the incidence of these untoward effects is not known, nor is it possible to predict which subjects wil experience such effects.

There have been recent suggestions that LSD may cause chromosomal damage in animals and humans, with implications of a teratogenic or carcinogenic potential. At the present time the volume and quality of evidence is not adequate to either confirm or rule out the possible adverse cytogenetic effect of LSD.

Addendum

Since the preparation of this manuscript, a number of reports and studies of the cytogenetic effects of LSD have been published.

Roux *et al*,[1] in an extensive controlled study of pregnant rats, mice, and hamsters given 5 to 500 micrograms per kilogram of LSD during gestation or organogenesis, found no increased incidence of malformed or stillborn fetuses. Aase *et al*[2] surveyed a small series of children whose mothers had ingested LSD in pregnancy, finding no increase in chromosomal abnormalities as compared with "control" infants of non-LSD-using mothers.

Two more case reports[3, 4] have appeared of deformed infants born to mothers who used LSD during pregnancy. Assemany and colleagues[3] report the case of an infant born with amputation deformities of the third finger of the right hand and the third toe of the left foot. The infant's mother had ingested unknown amounts of LSD during the pregnancy and had had three episodes of "hepatitis" during the 36 week gestation. These authors also mention three previously reported cases in which they feel similar defects possibly associated with LSD occurred. Eller and Morton[4] report the occurrence of spondylothoracic dysplasia in such an infant; this rare deformity has been previously seen only in children of closely contiguous marriages, presumably resulting from a recessive trait. In a third case report, Warren *et al*[5] describe a normal child born to a mother who used large doses of LSD numerous times during pregnancy.

These additional findings do not alter the conclusions presented in our review.

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From The Pamphlet Shelf

"What They Say About Chiropractic" is the title of the latest AMA pamphlet on the practice of chiropractic methods. Efforts have been made to draw together summaries of unbiased research done by various health agencies and organizations concerned with the well being of the retarded and the aging. Pamphlets are available at the Society headquarters from Leonard R. Tomat, Assistant Executive Director.

"Health Quackery" is an interesting collection of quack remedies used throughtout the years in the practice of deceit in health care. This informative pamphlet attempts to convince the public that quackery is as old as civilized man. Amusing and directly written the booklet was produced by the Department of Health Education and the Department of Investigation of the AMA.

Special Article

The Use of Drugs in Various Types of Cancer

David S. Fischer, M.D.

PART I

Progress in the palliation of far advanced cancer, most particularly metastatic cancer, has taken place largely in the years since the second world war. Starting with the development of nitrogen mustard and aminopterin, progress in the field has been quite rapid and remarkable. In recent years, some physicians have made a specialty of treating patients with drugs when their metastatic disease was no longer curable by surgery or irradiation and these physicians are called cancer chemotherapists. In contrast, anyone with a special interest in the study or treatment of cancer is now known as an oncologist.

Since much of the work in the field of chemotherapy has been experimental and exploratory, it has largely been conducted at university medical centers and in a few of the larger hospitals. With increased experience in the area, and as many of these early investigators have gone out into private practice, their combined experience is now available for the treatment of patients in private practice and not necessarily in the special clinics or university hospitals. In addition, as the knowledge of the various cytotoxic drugs has become more widespread among chemotherapists, and as the F.D.A. has approved more of them for use on a routine basis rather than with experimental protocols, chemotherapy has become commonplace and of age. This article will be an attempt to place it in perspective and indicate which tumors are amenable to palliative therapy, and what one in general can expect when a patient is referred to an oncologist for chemotherapy. The emphasis will be upon the use of standard F.D.A. approved drugs in private practice both in the office and the hospital. There is a voluminous literature relating to experimental drugs and their use in special research centers which we will *not* review at this time.

General Principles

When the patient is first seen in consultation by the chemotherapist, a relevant history and thorough physical examination is usually accomplished and the exact histological type of the malignancy, as well as its extent is ascertained whenever possible. Although chemotherapy can and has been given for an unspecified carcinoma or sarcoma, it is generally far more effective when the exact histological type of the tumor is known. In fact, we shall only discuss a few selected instances of this, as the results can only be evaluated in relation to definite tumors that have been histologically identified.

The patient is most often begun on therapy after a thorough workup in a hospital, but if this has previously been accomplished before the oncologist sees the patient, it is sometimes reasonable to begin chemotherapy in the office. In general, one does not begin until the patient is adequately hydrated and has a good urine output and the usually elevated uric acid level is falling. Since the advent of allopurinol (Zyloprim®), it is now relatively easy to insure that the uric acid will remain within normal limits. Since the vast majority of agents used for chemotherapy of cancer are cytotoxic and cause depression of the bone marrow, it is important either to be certain that there is no infection present or that any infection that is present is known by organism type and that it is sensitive to available antibiotics which the patient can tolerate. Transfusions are usually given when appropriate i.e. in the patient who is able to work and carry on his usual functions, transfusions are given when fatigue and shortness of breath limit these functions. In the more sedentary or bedridden patient, transfu-

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sions are usually given only for shortness of breath, severe anemia with a cardiac or coronary insufficiency, to replace acute blood loss, or to make it possible to give chemotherapy which would be contraindicated by a severe anemia. Hemolytic anemias which are frequently seen with chronic lymphatic leukemia and lymphosarcoma are best treated with appropriate doses of corticosteroids. Of course, with the corticosteroids, latent diabetes mellitus is sometimes unmasked and a tendency to infection with the usual bacteria as well as opportunistic organisms is also increased. Patients who are very near terminal are generally not accepted for therapy as their poor nutrition increases the risks of toxicity without much prospect of useful palliation. Patients should be started early, as soon as symptomatic. In general, the patient should not be advised of the planned therapy until the attending physician and the consultant have agreed on the plan of action, otherwise one might inadvertantly restrict the freedom of choice of the other.

Is Toxicity Necessary?

For some years, it had been a general concept in cancer chemotherapy that host toxicity was necessary to achieve a definite tumor response. Recently, an analysis of the relationship between host toxicity and tumor response was made by Bross et al,[1] using data from 956 patients receiving a variety of cytotoxic drugs. These investigators used several criteria to categorize host toxicity in testing its relationship to the incidence of objective tumor response, which was based on a 50% reduction of tumor size. They found that the proportion of responses was no higher among patients exhibiting signs of toxicity than among those free of toxicity. Their results suggest that there is not a close relationship between host toxicity and tumor response as generally believed, but rather that the physician must learn to give an optimal dose of therapy rather than push the drug to toxicity.

What to Tell or Not Tell the Patient

The controversial question of whether to tell the patient that he or she has a malignancy has not been resolved to everyone's satisfaction. After several years of experience on both sides of the issne, it seems to me that in medicine, as in life, honesty is the best policy. The patients today are too knowledgeable and too sophisticated to accept lies very readily. When one starts lying to a patient, it starts an entire chain of lies, and it is almost impossible to keep track of all the lies that one has told and, invariably, the patient loses confidence. Furthermore, if radiation is to follow the surgery, the patient would have to be very naive to believe anything other than that he or she had a malignancy. Both doctors and families are fooling themselves when they believe that just because they haven't told the patient the diagnosis, that the patient doesn't know it. Patients read books and have enough background and experience with life to know what cancer is all about and to know that, in general, their families and physicians may lie to them about it. The tragedy of this is that when the physician has lied to the patient, the patient loses confidence in the physician and cannot believe anything he says, even when subsequent discussions are truthful. In addition, the patient goes through a terrible loneliness in which he or she has no one to talk to because the patient is not supposed to know the truth and, therefore, can discuss it with no one. This is far more cruel than telling the truth, if the patient wishes to know the truth. If the patient does not want to know, and does not ask, then he should not have the diagnosis forced on him.

If one agrees that the patient has the right to know the truth, how should one present it? My own philosophy is to tell the patient just as much as he or she wishes and specifically asks to know. If the patient asks what the biopsy or operation showed, I usually tell him that it showed a tumor. The patient may then ask whether the tumor was malignant, but just as frequently, he may not. If he asks whether it was malignant, I usually indicate that it was and then the patient may go on to ask about spread, but at each point, I allow the patient the option of ceasing his questions. If he persists to the very end, he will then learn that the tumor was indeed malignant, that it has spread in terms of metastases and that it is beyond cure by either surgery or radiation. I never allow the subject to close without assuring the patient, however, that chemotherapy will be attempted and that there are high hopes that it will cause the tumor to shrink and that this will, hopefully, prevent pain and make the patient substantially better. I also point out that the doctor is not God and cannot predict the future and I never attempt to predict how long the patient will live or what the future course of the disease will be. All discussions should end with a reassurance to the patient that he is going to be cared for and that he will be protected from pain and undue suffering and that every effort is being made to insure his well being, and that he will not be abandoned by the chemotherapist. All too often, patients who have been diagnosed by a general practitioner and then referred to a surgeon and are then referred to a chemotherapist have an acute fear of abandonment. The chemotherapist must reassure them that he will not abandon them, but will continue to care for them along with the referring physician, who must participate in the care. It is a cardinal mistake for the primary physician to be excluded from the care of the patient even though he is not giving the chemotherapy per se.

Cancer of the Female Breast

It has been several years since this problem was reviewed by Dr. Goldenberg in this journal, but the major avenues of approach have not changed very much.[2] The management of the female with unresectable or metastatic carcinoma of the breast generaly falls into two categories, the patient who is premenopausal or recently menopausal, and the patient who is postmenopausal by some time interval. Some authors include in the premenopausal group those who are only five years postmenopausal and other authors include those who are ten years postmenopausal and separate the two groups at the ten year mark. In general, the premenopausal patient with metastases should have an oophorectomy. Whether this should be done as soon after her diagnosis of metastatic malignancy as possible, or only when she has evidence of progression is controversial. Oophorectomy usually gives a response in 50% of patients with recurrence, and this remission may go on for weeks, months, or even years. Further therapy should not be attempted until there is some evidence of relapse. At that time, one may go on either to an adrenalectomy, or sex hormone therapy. The adrenalectomy may be by the surgical technique, or one may perform a "medical adrenalectomy" by giving moderate doses of prednisone or other corticosteroids to suppress the function of the adrenal. This is usually somewhat less successful than surgical adrenalectomy, but it frequently succeeds and is far less traumatic. In instances when adrenalectomy of any sort is a failure, some physicians go on to hypophysectomy. I have had very little experience with this and the literature on it is quite controversial. The procedure is difficult and the remission rate depends on whose article is used for reference, as some excellent responses have been reported. Certainly, it requires an expert neurosurgeon and a team prepared to administer a wide spectrum of replacement therapy. It is usually far easier to go on to exogenous hormonal therapy.

Most patients in this younger premenopausal group will respond far better to androgens[3] than to estrogens since they are already producing moderately large amounts of estrogens. Should androgens fail, some clinicians go on to estrogens, but I avoid this because I have seen a few patients whose disease apparently accelerated after estrogens. Hence, I generally go on to chemotherapy at this point.

For the postmenopausal woman who is at least ten years postmenopausal, oophorectomy is simply not indicated. In most instances, the ovaries are producing little or no estrogen at this time and a vaginal smear will show no cornification. These patients are generally begun on androgens, particularly if they have bony metastases and have a good expectation of gaining remission. Many oncologists prefer to start these patients on estrogens to change the hormonal environment and this is especially successful in the case of skin and nodal disease. The studies of some of the published groups would tend to indicate that estrogens are generally more successful in the postmenopausal patient, but the recent studies of the combined breast cancer group, as reviewed by Segaloff,[4] would indicate that androgen therapy is the preferred hormonal approach in virtually all cases. Following relapse on androgens, they generally go on to either an adrenalectomy, or corticosteroids to produce a "medical adrenalectomy". Following relapse from this, chemotherapy is again the treatment of choice for systemic disease, and local radiation for local recurrences producing pain or threatening to cause pathological fractures. Many therapists feel that the relatively lower incidence of response to hormonal therapy in patients with visceral metastases indicates that chemotherapy should begin early in these patients.

Chemotherapy has been most successful with 5-fluorouracil (5-FU), which gives a 40 to 50% remission rate and seems to cause the most prolonged remissions. Although it gives a transitory depression of the bone marrow, usually the bone marrow recovers adequately if the 5-FU is given carefully. The alkylating agents give about the same rate of remissions but these are usually not as long lasting as those with 5-FU and the bone marrow does not recover as well. Hence, I tend to begin therapy with 5-FU. Some clinicians find that it is more convenient to start with an alkylating agent that can be given orally, like chlorambucil (Leukeran®), or cyclophosphamide (Cytoxan®). The alkylating agents will often give a second remission after a previous failure with 5-FU, but the reverse occurs less often. When both 5-FU and the alkylating agents no longer give a response, then vincristine (Oncovin®), or methotrexate may be used and give responses in a smaller percentage of cases.

Since breast cancer is now the most common single cancer among women is the United States with well over 60,000 new cases each year, virtually every physician who sees many patients will encounter such a malignancy. It is essential that these patients be treated surgically when at all possible, but since more than half of them will proceed to metastasis and ultimately die of this, it is most important that they get aggressive radiation and/or chemotherapy, because life can be prolonged in many cases for five, ten, or even fifteen years with known metastases. No woman should be denied the potential benefits of chemotherapy in breast cancer, because even the most hopeless cases sometimes respond most dramatically.

Cancer of the Colon and Rectum

This is one of the most common forms of cancer and accounts for some 50,000 deaths annually. The majority of these cancers are detectable through procto-sigmoidoscopy. Therefore, a high proportion of these deaths could be averted by early diagnosis and treatment of the disease. However, even when the disease has reached a point where it is either unresectable, or metastases have been left behind, palliative therapy is still available. In cases of rectal lesions, X-ray therapy is sometimes helpful, although extensive experience has shown that most of these tumors are resistent to such treatment. Almost all colon adenocarcinomas are resistant to radiation therapy. Prior to 1957, it was observed that 5-fluorouracil (5-FU) produced regression of lesions of this tumor. Since then, extensive work has been done, most particularly at the University of Wisconsin, where the drug was synthesized by Heidelberger and tested clinically by Ansfield and Curreri. After treating well over a thousand cases, they came to the conclusion that 5-FU therapy should be employed as soon as possible following surgery when the patient is again in nitrogen balance. This generally means two to three weeks postoperatively, depending upon the nature of the surgery. Naturally, in uncomplicated resections of the colon or rectum, where the lesion did not penetrate to the serosa and all the regional glands were negative on microscopic examination, no chemotherapy is given since there is no evidence of remaining disease. In the extensive Wisconsin series, objective (*measurable*) regressions were demonstrated in 17% of all cases and very definite palliation of a nonmeasurable type was demonstrated in an additional 17% so that fully one third of all patients had significant responses to chemotherapy with 5-FU.

In these studies, 5-FU was usually given at a level of 12 mgs. per kilogram per day for five days and then at a level of 6 mgs. per kilogram every other day until toxicity was noted. They then repeated their therapy at monthly intervals. We started using this regimen, but eventually evolved to a program of using this as our initial course of therapy, but thereafter giving the patient approximately 500 to 1,000 mgs. of 5-FU at weekly intervals as judged by the response of the white count to this therapy. A similar program has recently been published by Jacobs, Luce and Wood.[6] In our hands, the response rate has been approximately 40%. Equivalent results have been reported with the use of 5-fluoro-2-deoxyuridine (5-FUDR). However, thus far, this drug has not been released by the F.D.A. and since it is so expensive, it is unlikely that it will come into widespread use. Several groups have reported that the results are no better than with 5-FU. In a small number of cases where 5-FU systemically has been unsuccessful, intraarterial therapy has been very useful. Sullivan and his colleagues[7] have reported the greatest success with this technique using 5-FU.

When 5-FU or 5-FUDR have ceased to be effective, no standard drug has been found to be useful. A variety of experimental drugs are being tested, but the patient must, of course, know that these are nonstandard and has to give an informed consent for an experimental protocol. These are done only in a university hospital or a similar research oriented institution. At present, the most promising experimental drug for these malignancies appears to be 1,3, Bis (B-chloroethyl)-1-nitrosourea (BCNU).

Cancer of the Upper Gastrointestinal Tract

Malignancies of the esophagus are most generally squamous in cell type and these are most frequently treated by radiation therapy. In the hands of a skillful radiation therapist, response rates often run as high as 50%. When radiation therapy is no longer effective, chemotherapy may be tried, but the response rates have been quite low, averaging 5 to 10%. The drug most often used is methotrexate. In some cases, alkylating agents like cyclophosphamide (Cytoxan®) have also given some successes.

Cancer of the stomach is most usually adenocarcinoma and the drug which is most effective here is 5-FU used in the same way as already described for adenocarcinoma of the colon. The Japanese have also reported some success with Mitomycin-C, but thus far, this has not been confirmed in the

United States by any sizable studies. The response with 5-FU is about 20 to 30%.

The next most common tumor of the stomach is a lymphoma or a reticulum cell sarcoma and these frequently give a very nice response to alkylating agents (to be discussed later in the section on Hodgkin's Disease and malignant lymphoma). Small bowel malignant tumors are extremely uncommon. When they do occur, the most common is adenocarcinoma. This is treated with 5-FU and favorable results occur in about the same incidence as with stomach. Lymphomas also occur in the small bowel and are amenable to therapy to be described later. Malignant carcinoids usualy occur in the distal ileum and in the appendix. They may metastasize to the liver causing a typical carcinoid syndrome. These have been treated with some very favorable results with either cyclophosphamide or dactinomycin (Cosmegen®).

The liver is a frequent site of metastatic disease, especially from the gastrointestinal tract, the breast, or the lung. When the tumors are from the GI tract and are adenocarcinomas, they are most generally treated with 5-FU systemically. When the tumor is isolated to the liver and the primary has been entirely removed, then arterial infusion should be considered. The hepatic artery may be cannulated and 5-FU pumped into it with a small, completely portable pump, which allows continuous infusion on an outpatient basis. Such patients must be very carefuly followed and supervised, but in some series, objective tumor response has been seen in 80% of cases.[8]

Primary hepatoma is treated with 5-FU in the usual fashion. Since it is usually complicated by cirrhosis of the liver, it is hard to really evaluate the therapy. It is well known that 5-FU is detoxified in the liver and therefore, full doses cannot be given under most circumstances if cirrhosis is present or if enough liver function has been compromised by the extensive tumor. No better therapy, however, has been evolved as yet and 5-FU remains the drug of choice.

Pancreatic carcinoma is usually diagnosed very late because of the inaccessibility of the pancreas to the usual diagnostic procedures. When seen, the tumor is most frequently already metastatic and surgery is seldom of value. Treatment with 5-FU has been successful in a reasonable number of cases and the overall response is approximately 30%. Objective remissions are hard to evaluate because of the protected position of the tumor, but the severe back pain, which requires high doses of narcotics is frequently ameliorated or even abolished by therapy with 5-FU. One recent study[9] suggests that the best results in pancreatic adenocarcinoma are obtained when 5-FU is combined with radiation therapy. The series was small but highly suggestive and additional studies will be needed because there is already one study which fails to comfirm this. The very rare insulin secreting tumors and the gastrin secreting tumors (Zollinger-Ellison syndrome) are now being recognized more frequently and therapy has been attempted with a variety of drugs, but it is still too soon to evaluate the small number of cases adequately treated.

Gallbladder carcinoma is very unusual, but when seen, it is usually of the adenocarcinoma or squamous cell carcinoma type. The adenocarcinomas are treated with 5-FU in the usual manner with a 20 to 30% response rate. The squamous cell carcinomas can be treated with methotrexate or cyclophosphamide, with slight success. Hepatic artery infusion has been attempted for some cases, but it is too early to evaluate the results.

Tumors of the Female Genital Tract

Cancer of the ovary is an increasingly common malignancy in women, rapidly catching up with carcinoma of the cervix. Although these tumors are difficult to diagnose, they are frequently somewhat indolent so that even a very large tumor is sometimes resectable. However, many of these tumors are unresectable and the surgeon must leave behind known tumor, particularly in the cystic tumors, which sometimes rupture prior to surgery or at surgery. Most of the tumors of the ovary are amenable to radiation therapy and the adenocarcinoma, in particular, responds quite well. However, following recurrence of tumor that has been irradiated, chemotherapy gives another opportunity for reasonably good palliation, particularly with 5-FU or an alkylating agent. The 5-FU is usually used in the same dose as that specified for gastrointestinal tumors, such as that of the colon and the results have been very gratifying. If ascites is present, some authors instill thio-TEPA intraperitoneally after the fluid is withdrawn. Although some authors have advocated use of nitrogen mustard in the free peritoneal cavity, we have seen several instances of subsequent intestinal obstruction and we have avoided this practice. If after careful follow-up there is no evidence of progression of the disease, then maintenance 5-FU is given until such time as the tumor becomes resistant. The patients who become resistant to 5-FU can later be treated with alkylating agents with a second remission. Of course, alkylating agents are radiomimetic and repeated courses may produce permanent bone marrow damage. When 5-FU is given skillfully, it usually does not produce permanent marrow suppression. Hence, the desirability of using this order of therapy, 5-FU first, and alkylating agents later. To a certain degree, cyclophosphamide is less toxic than the other alkylating agents and one can frequently give long term cyclophosphamide therapy with minimal bone marrow toxicity because it tends to spare the platelets and red cells more than the other alkylating agents. We think that this reduced toxicity is due to the fact that cyclophosphamide is inactive as it is given and becomes active in the body when the phosphoamide bond is severed within the cell and the drug then releases nitrogen mustard locally, which is the cytotoxic agent. Both thio-TEPA and chlorambucil have been used extensively, particularly by gynecologists, and there are several large series using these drugs. Phenylalanine mustard (Alkeran®, Sarcolysin®, melphalan) has been reported to be of value in the treatment of ovarian carcinoma, but it is just another alkylating agent that produces severe bone marrow depression. Within my own experience, the best results have been with cyclophosphamide and second best with chlorambucil.

Frequently, combined chemotherapy and radiotherapy are more efficacious than either alone. Most frequently, 5-FU is combined with the radiotherapy to minimize bone marrow toxicity. Should leukopenia supervene, then the 5-FU is withheld and X-ray therapy alone is given. When the bone marrow recovers, then the 5-FU may be reinstituted.

Stilbestrol therapy has been advocated by Long and Evans.[10] In their study, four of nine patients showed objective and subjective improvement with stilbestrol. The oral dose ranged from 15 to 30 mgs. per day, averaging 20 mgs. per day, according to the tolerance of the patient. This therapy has been particularly useful in those patients whose bone marrow has been compromised by cytotoxic therapy or pelvic radiation. The results remain to be demonstrated by other groups.

Cancer of the cervix with dissemination or recurrence is generally treated with radiation therapy. When this has failed and there is still evidence of aggressive disease, chemotherapy may be attempted with either 5-FU or an alkylating agent such as cyclophosphamide. The results have not been terribly dramatic with these agents and recently, several studies with high dosage methotrexate have been attempted with some suggestively favorable results, but these need further confirmation. In patients with compromise of the ureters and an elevated BUN, methotrexate is extremely dangerous, as its major route of excretion is by the kidneys. Thus, cervical carcinoma may respond to chemotherapy, but this is certainly not routine therapy at present.

Cancer of the endometrium has most recently become responsive to hormonal therapy even in cases of disseminated disease.[11] The pulmonary lesions respond better than visceral lesions or bony lesions, but it is always worthwhile to treat these patients. The best progestational agents that can be given in high dose are either 17-alpha-hydroxyprogesterone caproate (Delalutin®) in a dose of a half gram weekly, or else medroxyprogesterone acetate (Depo-Provera®) in doses of approximately 500 mgs. per week. These two hormones have been quite successful in approximately 30% of cases. Both of these agents are not cytotoxic and have almost no side affects and should be tried in all cases when other methods fail. It is still too early to have any large series of cases to evaluate results. When these fail, cytotoxic therapy may be tried with an alkylating agent. but the response rate has been of a low magnitude.

End of Part I

(This is the first of a series of two articles)

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Electrocardiogram of the Month: P-waves

Yale-New Haven Hospital
New Haven, Connecticut

Prepared by
HYMAN M. CHERNOFF, M.D.
Associate Professor of Clinical Medicine,
Yale School of Medicine
Director, Dept. of Electrocardiography
Memorial Unit, Yale-New Haven Hospital

Atrial depolarization gives origin to the P-wave. Atrial repolarization produces a deflection in the electrocardiogram which is opposite in polarity to the P-wave and is referred to as the T_P or T_A-wave. Usually the T_P-wave is not seen in body surface leads because of its low amplitude and also because it is obscured by the much larger deflection of the oncoming QRS complex. T_P becomes manifest in AV block when the QRS is far removed from the P-wave.

Fig. 1 is an electrocardiogram from a young patient with congenital complete AV block. The atrial rate is 85 to 100 per minute while the ventricular rate is 48 to 50 per minute. When the QRS is sufficiently removed from P, the T_P is exposed and is seen to be of low amplitude, and of opposite polarity from P. Note that when a P-wave falls just before or during QRS, that then the T_P occurs immediately after the QRS and alters the configuration of the ST segment. In this instance the ST segment displacement represents atrial repolarization and not altered ventricular repolarization.

When the atrial rate is accelerated, atrial repolarization is hastened and T_P can be recognized as a displaced PR segment in a direction opposite to that of P. This phenomenon can be found during fever, after exercise, during sympathetic overactivity, in hyperthyroidism, or following ingestion of sympathomimetic drugs. Fig. 2 is the electrocardiogram of a 22 year old patient with hyperthyroidism. There is a sinus tachycardia of 140 per minute. Note the downward slope of the PR segment in leads 1, 2, VF, V2-V6 and the upward slope in lead VR. The QRS complex now appears to arise below the isoelectric line in leads 1, 2, and in the chest leads. The junction of the ST segment is likewise displaced by T_P. This is pseudo-displacement and is due to atrial repolarization. Similar junctional type ST displacement may be noted following the exercise tolerance test and should not be mistaken as evidence of myocardial ischemia.

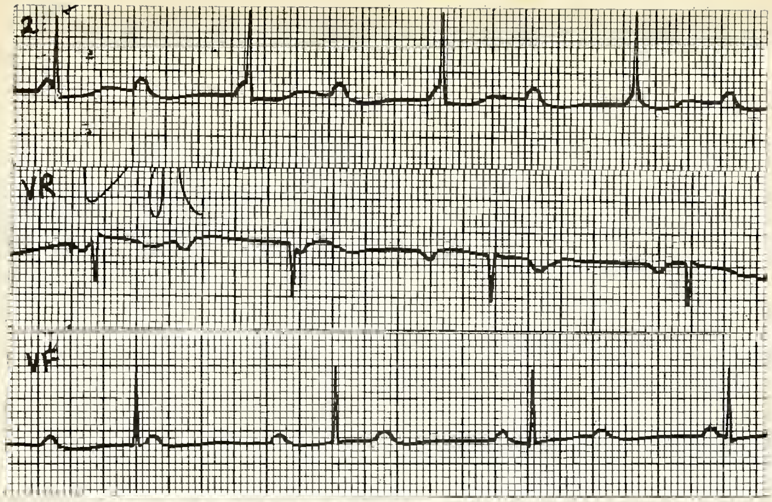

FIG. 1

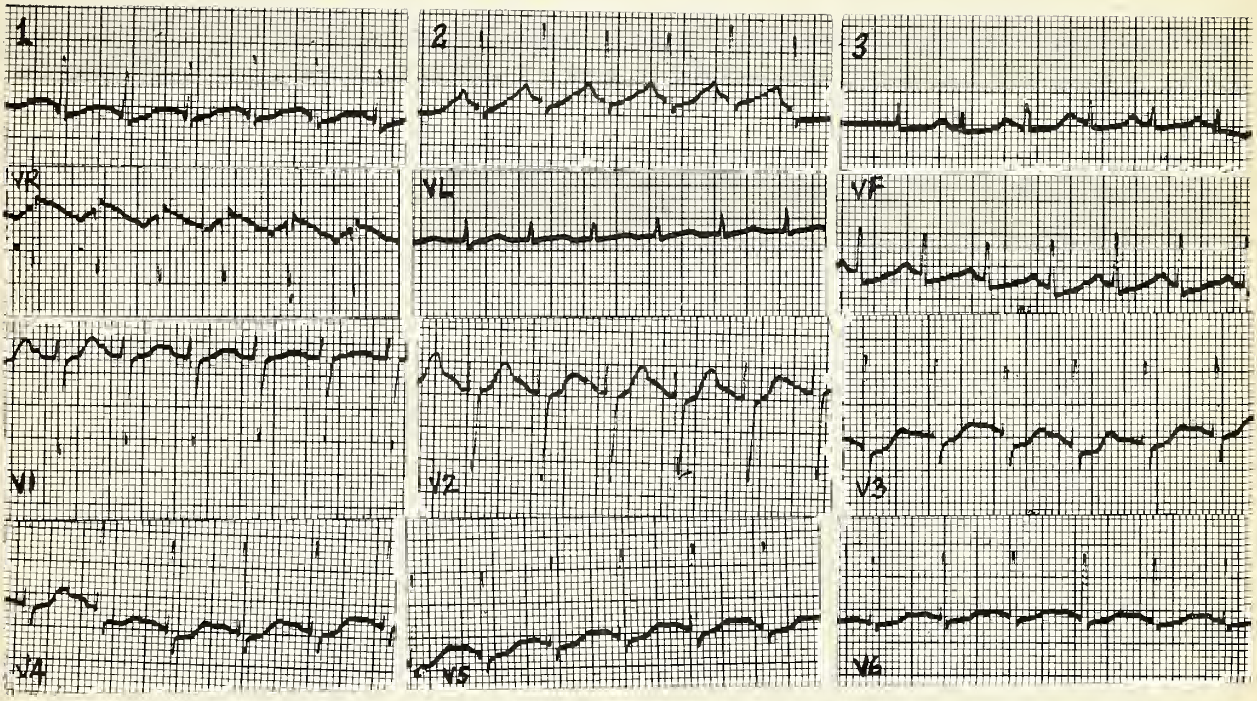

FIG. 2

PUBLISHED TO REPLACE A PREVIOUS ADVERTISEMENT WHICH THE FOOD AND DRUG ADMINISTRATION CONSIDERED MISLEADING

The Food and Drug Administration has requested that we bring to your attention a recent promotional campaign for Garamycin Injectable (gentamicin sulfate) which featured a nationwide *in-vitro* hospital survey involving a comparison of sensitivity patterns of Garamycin Injectable and seven other antibiotics.

The FDA considers the advertising misleading in several respects such as:

The *in-vitro* chart contained in the ads, which compared Garamycin Injectable with seven other antibiotics, implied that Garamycin Injectable is clinically more effective than the seven other compared antibiotics. THE FACTS ARE (1) THAT DIRECT EXTRAPOLATION OF NONCLINICAL FINDINGS TO CLINICAL EFFECTIVENESS IS UNWARRANTED, AND (2) THAT THE ADVERTISED *IN-VITRO* COMPARISONS DO NOT CONSTITUTE A VALID BASIS FOR SUGGESTING THAT GARAMYCIN INJECTABLE HAS GREATER CLINICAL EFFECTIVENESS THAN THE COMPARED ANTIBIOTICS.

The *in-vitro* chart and information contained under the ad heading, "Indications" presented *in-vitro* data results in such a way as to imply that the drug is indicated for Gram-positive bacteria, such as *Staphylococcus aureus.* GARAMYCIN INJECTABLE IS NOT APPROVED FOR INFECTIONS DUE TO ANY GRAM-POSITIVE ORGANISMS.

We emphasize that Garamycin Injectable is approved for use only in infections due to susceptible strains of gram-negative bacteria, including Pseudomonas aeruginosa, and species of indole-positive and indole- negative Proteus, Escherichia coli, and Klebsiella-Aerobacter.

Schering

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# injection

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BRIEF SUMMARY

INDICATIONS GARAMYCIN Injectable is clinically effective in infections due to susceptible strains of gram-negative bacteria, including Pseudomonas aeruginosa, and species of indole-positive and indole-negative Proteus, Escherichia coli, and Klebsiella-Aerobacter. Bacteriologic studies should be conducted to identify the causative organism and to determine its sensitivity to gentamicin sulfate. Sensitivity discs of the drug are available for this purpose. If the susceptibility tests indicate that the causative organism is resistant to gentamicin sulfate, other appropriate antibiotic therapy should be instituted.

This drug should be limited to the treatment of serious infections caused by gram-negative bacteria, particularly Pseudomonas aeruginosa, Proteus and other susceptible organisms, with due regard for relative antibiotic toxicity. Therefore, the drug should be considered for use against gram-negative: 1. Bacteremia; 2. Infected surgical wounds; 3. Severe soft tissue infections, including burns complicated by sepsis; 4. Respiratory tract infections; and 5. Selected cases of urinary tract infection.

CONTRAINDICATIONS GARAMYCIN Injectable is contraindicated in individuals with a history of hypersensitivity or toxic reactions to gentamicin.

WARNINGS **Patients receiving treatment with GARAMYCIN should be under close clinical observation because of the toxicity associated with the use of this drug. Ototoxicity, vestibular and auditory, can occur in patients, primarily those with pre-existing renal damage, treated with GARAMYCIN Injectable, usually for longer periods or with higher doses than recommended.**

GARAMYCIN Injectable is potentially nephrotoxic, and this should be kept in mind when it is used in patients with pre-existing renal impairment. Kidney function diminished by infection of the upper urinary tract may, however, improve during effective treatment with GARAMYCIN Injectable.

Concurrent administration of potentially ototoxic drugs such as streptomycin and kanamycin or of potentially nephrotoxic drugs such as polymyxin, colistin, and kanamycin with gentamicin sulfate has not been shown to afford any clinical advantages and, moreover may result in additive toxicity. Monitoring of vestibular, cochlear, and renal function will provide guidance for therapy in such cases.

PRECAUTIONS In patients with impaired renal function in whom serious infection develops, serum concentrations of the drug may rise, with consequently increased risk of ototoxicity. In these patients or in those in whom recommended dosage or duration of therapy must be exceeded as a life-saving measure, routine studies of kidney function should be performed when possible. These may be supplemented by evaluation of the vestibular and auditory function and measurement of serum concentration of the drug when feasible. Serum concentration of gentamicin should be maintained below the range of 10-12 mcg./ml. to reduce risk of ototoxicity.

Ordinarily, treatment should not be given for more than 7 to 10 days or be repeated unless required for serious infection not responsive to other agents.

As with other antibiotics, treatment with GARAMYCIN Injectable may occasionally result in overgrowth of nonsensitive organisms. If superinfection occurs, appropriate therapy is indicated.

Safety for use in pregnancy or the potential for fetal ototoxicity or nephrotoxicity have not been established. Studies in pregnant animals have not revealed teratogenic or ototoxic effects in the fetus. GARAMYCIN Injectable should not be used in pregnant patients or in women of childbearing age unless its use is deemed advisable by the physician.

ADVERSE REACTIONS The overall incidence of ototoxicity considered related to treatment with GARAMYCIN Injectable was 2.8 per cent (16 of 565 patients). Contributory factors (two or more factors were relevant to most patients) were as follows: 10 had azotemia, 10 received a total of 1 gram or more of the drug, 7 had recently received other potentially ototoxic antibiotics (streptomycin or kanamycin), and 5 were over 60 years of age. Six also had decreased high-tone hearing acuity, which returned to or toward normal in the 4 patients retested.

Analysis of BUN data indicated that 4 (2%) of 172 patients showed increases in BUN that were probably related to treatment with GARAMYCIN Injectable. Of 20 increases probably or possibly related to treatment, 7 were reversible, 9 occurred in terminal patients, and 4 had no follow-up.

Other adverse reactions associated with treatment were one instance each of urticaria, decreased hematocrit, and reversible depression of granulocytes with normal bone marrow. Other rarely reported and possibly treatment-related adverse reactions were anemia, increased reticulocyte count, rash, purpura, drug fever, hypotension, convulsions, twitching, salivation, nausea, vomiting, increased transaminase activity (SGOT or SGPT), increased serum bilirubin, decreased serum calcium, and joint pain.

PACKAGING GARAMYCIN Injectable, 40 mg./cc., 2-cc. multiple-dose vials, for intramuscular administration.

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X-Ray of the Month

Phantom Lung Tumor

Section of Chest Diseases

Yale-New Haven Medical Center

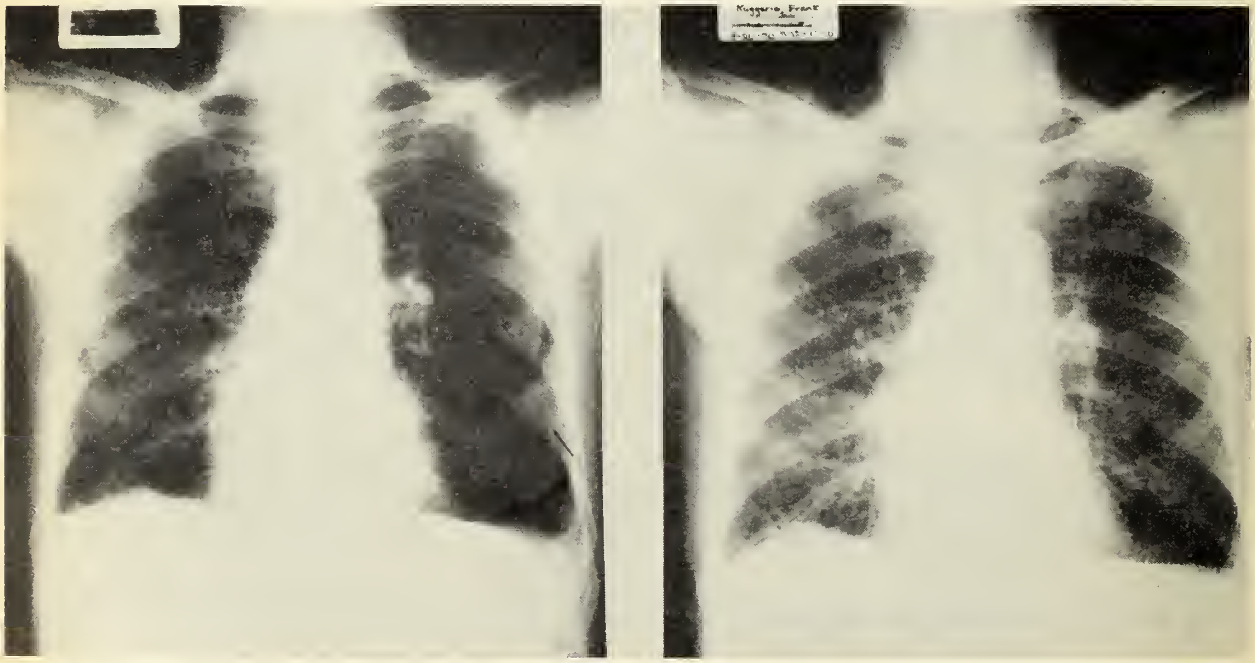
Arnold B. Rilance, M.D., Director, Winchester Chest Clinics

F. R., #B3-31-20, a white male, age 79 years, was found to have renal tuberculosis in August, 1957, for which he was treated with a course of Isoniazid and sodium paraminosalycilic acid. He made an uneventful recovery.

Subsequently he was seen in the Urology Clinic and the Winchester Chest Clinic of Yale-New Haven Hospital because of complaints due to prostatic hypertrophy and episodes of mild congestive failure. X-rays of his chest never demonstrated tuberculosis at any time and changes at the base of the right lung were considered to be due to pleural thickening.

On 7/23/70, a routine chest film was made and demonstrated a low density mass about 3-4 cm. in diameter situated over the lateral portion of the left anterior fifth rib. The X-ray density was thought to be either intrapulmonary or pleural in nature.

At operation, a 4 cm. seborrhiac dermatosis was removed by curettage and electrodessication. The operation was uneventful and a complete cure of the phantom lung tumor was achieved.



In the film to the left a sharply outlined slightly lobulated density is outlined by arrows overlying the anterior end of the left 5th rib. The lesion has all the usual characteristics of an intrapulmonary neoplasm.

After removal of a large pedunculated skin lesion on the back of the left hemithorax, the second film shows this density to have completely disappeared. This can be called a "phantom lung tumor".

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The following are excerpts from a speech on "Putting Womanpower to Work for Medicine" that was made by C. A. Hoffman, M.D., Trustee, American Medical Association in Philadelphia on October 3rd, 1970.

What is a doctor's wife? One woman expressed the perils of doctors' wives this way:

So pity the spouse in the doctor's house,
The spouse of the house sublime,
For though she is wed, it may truly be said,
She is husbandless most of the time.

I am sure all of you can attest to the truth of those words. Being a doctor's wife is not as glorious as everyone makes it out to be. But would you have it any other way? I am sure when you stop to think of it, you realize how important it is for a doctor to have a wife who backs him up, cheers him when he needs it, encourages him when his confidence is fading, and talks medicine with him when he needs a listening-post.

In addition, as a doctor's wife, you have a social task to perform. Your Woman's Auxiliary is performing vital services to the community that show the stuff the medical profession is made of.

Shakespeare, put himself out on a limb when he said, "Frailty, thy name is woman." He could not have been talking about the Woman's Auxiliary. A frail woman could not handle the job that you perform . . . nor could she cope with the problems that arise in an organization like yours. The AMA has problems which it knows you have been helping to solve. It would be easy for me to list them, but I am sure you know which problems exist, so I will save my breath and your time. Right now, there are two more basic problems that require consideration. The first is what we might call "internal public relations." By that I mean letting your auxiliary members know why, when and how very much they are needed in the organization—on the county as well as state and national levels.

Be informed and persuasive in competing for the interest, time, services and efforts of doctors' wives in developing our imput to the health care system and community life.

The category of members-at-large should be reevaluated from time to time so that their potential may be fully utilized.

Give all of your members a concrete reason to work for the betterment of medicine through the auxiliary and no one will have the chance to say, "I have more important things to tend to." Chances are you have heard that excuse a hundred times if you have heard it once. But you need your members, so let them know what vital links they can be. As well as contending with the problem of encouraging existing members to become more socially conscious and active within your county groups, it seems that recruiting new members has become a hard job also. Recruiting a doctor's wife should deal with the why's and wherefore's of the auxiliary and how much help is needed to support the medical profession.

And this is your editor's comment: "Go to it girls, from past experience, we know you can!"

CSMS EMERGENCY MEDICAL CARD

Physicians wishing to give patients an emergency medical card may obtain a supply from the CSMS office. This card was designed by the Society to provide identity information with notations about physical conditions which might affect the manner of emergency treatment.

AROUND THE STATE

Participants at the recent Symposium on Ocular Trauma: Back Row—Claes Dohlman, M.D., Retina Foundation, Boston, Mass.; David Paton, M. D., Johns Hopkins University, Baltimore, Maryland; Ralph Rosenthal, M.D., Walter Reed Hospital; Nathaniel Bronson, M.D., Southampton, Long Island; Irving Leopold, M.D., Mt. Sinai School of Medicine, New York City; Marvin Sears, M.D., Yale University School of Medicine; Front Row—Daniel Albert, M.D., Yale University School of Medicine; Harvey Thorpe, M.D., Pittsburgh, Pennsylvania; Alston Callahan, M.D., Birmingham, Alabama; Morton Goldberg, M.D., University of Illinois; Stuart Brown, M.D., Cornell University College of Medicine.

An all day symposium on ocular trauma brought together in New Haven on Friday, October 30, 1970, some of the outstanding ophthalmologists in the country. Sponsored by the Committee on Eye Care of the Connecticut State Medical Society, the Department of Ophthalmology at Yale University School of Medicine, and the Section on Ophthalmology of the CSMS, this Fifth Joint Clinical Meeting held their sessions at the Fitkin Amphitheatre at Yale.

The morning session was highlighted by a paper presented by Alston Callahan, M.D., of Birmingham, Alabama. Dr. Callahan's specialty is plastic surgery as it deals with the eye lids and the ocular orbit. This subject was also discussed by David Paton, M.D., Associate Professor of Ophthalmology at Wilmer Institute at Johns Hopkins University in Baltimore, Maryland. Chairman of the discussion that followed was Rocko M. Fasanella, M.D., of the Yale Medical School.

"Cornea and Chemical Injuries" was discussed by Stuart I. Brown, M.D., of Cornell University College of Medicine, and Claes H. Dohlman, M.D., of the Retina Foundation of Boston. Dr. Dohlman is responsible for research activities and basic study of the cornea and is known for his application of plastic materials in diseases of the cornea. The discussion leader following the presentation was Daniel M. Taylor, M.D., of New Britain.

After lunch at the Faculty Lounge, Harvey E. Thorpe, M.D., of Pittsburgh, Pennsylvania, Nathaniel R. Bronson, M.D., Southampton, Long Island, and A. Ralph Rosenthal, M.D., of the Walter Reed Hospital discussed "Intraocular Foreign Bodies." Dr. Rufus O. Howard of Yale chaired the discussion.

Marvin L. Sears, M.D., of Yale, and Morton F. Goldberg. M.D., of the University of Illinois, and David Paton, M.D., of Yale, analyzed "Intraocular Surgery" with Dr. Arthur C. Unsworth of Hartford as the discussion leader.

William B. Brewster, Jr., M.D., of Hartford presided over the business meeting of the CSMS Section of Ophthalmology before the group adjourned to the Park Plaza Hotel for dinner and a program by Irving H. Leopold, M.D., of New York City and David Albert, M.D., of Yale. Dr. Leopold is presently Professor and Chairman of the Department of Ophthalmology at the Mt. Sinai School of Medicine and recently was named the President-elect and Dean of the Women's College of Medicine in Philadelphia. Dr. Andrew S. Wong, of New Haven, was the chairman for the after dinner program.

New Haven County

The 187th Semi-Annual Meeting
New Haven County Medical Association

The 187th Semi-Annual Meeting of the New Haven County Medical Association was held at the Waverly Inn in Cheshire, Conn. on Thursday, October 22, 1970. 408 members registered and 268 dinners were served in the evening. President Stewart J. Petrie welcomed the members and then a moment of silence was observed in memory of our departed members who were:

Samuel A. Jaffe, 1913-1970
Martin J. Kligerman, 1936-1970
Robert R. Nesbit, 1903-1970
Charles G. Wilson, 1895-1970
Ralph DeCristoforo, 1910-1970

By unanimous vote the following physicians were elected to membership:

Daniel Myron Albert—New Haven
Claude Andre Blain—Waterbury
Benito Italo Bonaccorsi—Waterbury
John Edward Boyd—New Haven
Gerard N. Burrow—New Haven
Aldo R. Chavez—Waterbury
Richard A. Cooper—New Haven
Andrew Monroe Diggs—Waterbury
Steven L. Eisen—Waterbury
Gerald Fishbone—New Haven
Graeme Lord Hammond—New Haven
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Milton Huyett Sangree, Jr.—New Haven
Henri J. Schapira—New Haven
Thomas J. Spackman—New Haven
Herbert Suesserman—Hamden
Robert J. Touloukian—New Haven
Augustus Aaron White—New Haven
Arnold Eugene Zeff—New Haven

Transfer from Out of State Counties:

Dara B. Dubash—New Haven
Ethem Y. Kuzucu—Middlebury
Richard Martin Levy—Derby

Connecticut State Medical Society President Morris A. Granoff stressed the contrary direction being taken by CRMP and RMP when compared to the intent of the original legislation. He hoped the Council would be able to demonstrate success in dealing more effectively with the obvious discrepancies in the planning group's activities. Connecticut State Medical Society Executive Director William R. Richards and later guest speaker J. Alfred Fabro of Torrington both discussed the difficulties facing the medical profession in the field of Malpractice Insurance.

Mrs. Boris Rifkin, President of the Women's Auxiliary of New Haven County and Mrs. John Mendillo, President of the Connecticut State Medical Society Women's Auxiliary both addressed the membership. Both speakers outlined their current activities and each called upon the New Haven County Medical Association for closer coordination and mutual assistance.

President Stewart J. Petrie reported that greater Association attention is needed in the following areas:

1. Pollution of the environment.
2. Town-gown relationships.
3. -Drug Abuse.
4. Passage of a Health Education Bill by the Connecticut Legislature.

Dr. Louis Cappucci reported that the Public Relations Committee is making progress. He praised the work of Mr. Arthur Schuman our Public Relations Director and Dr. James H. Root, Jr. our editor. Doctor Cappucci pointed out that the

Speakers Bureau has been formed, two local area radio programs are running smoothly in Waterbury and the Naugatuck Valley areas, the President's Newsletter is mailed monthly, the Quarterly Journal "Issues and Insights" is mailed quarterly and will soon be self-sustaining, and improved local society and Connecticut State Medical Society relationships are evolving.

Dr. Jerome K. Freedman, guest speaker, outlined some of his experiences and thoughts about the problems presented by an ever-expanding proliferation of "Health Planning" groups. Dr. Russel K. Fuldner elaborated on some of these matters, also.

Dr. Bernard A. Burnham outlined Connecticut State Medical Society legislative goals for 1971 and spoke on the resurgence of COMPAC in the areas of political education.

Dr. Howard Spiro outlined the beginnings of an effort to improve town and gown relationships.

All told, 22 committee reports were approved during the meeting.

By due parliamentary process six members, one from each local geographical area, were elected to the Nominating Committee. They are:

Herbert Weisberg—Waterbury
Willem Van Eck—East Shore
Oscar Rogol—Naugatuck Valley
Irving Shiffman—Meriden
Albert J. Howard—New Haven
Waldo E. Martin—West Shore

Three By-Laws changes were adopted, one rejected, and three referred back to the By-Laws Committee. The amendment that was rejected would have called for expulsion from membership as a penalty for non-attendance at one out of every five annual or semi-annual meetings. The consensus that led to its rejection was that expulsion would be too severe a penalty. Additionally, a By-Laws change was laid on the table by Dr. Luca E. Celentano to be voted on March 25, 1971 which calls for abolition of compulsory attendance.

Following a social half-hour, 268 roast beef dinners were served to an enthusiastic gathering of members and spouses. The entertainment was well received in the form of memory expert and comedian Mr. Irv Wermont and the raffling of door prizes by the Program Committee Chairman Dr. Anthony Mancini, who was commended for his fine program.

Respectfully submitted,
William L. West, M.D., Clerk

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Watching for Carcinogens

(*Nature* 227, 990, Sept. 5, 1970). The epidemiological section of the International Agency for Research on Cancer continues to digest statistics and produce uncomfortable correlations. Cancer of the esophagus in Curacao seems to be related to the consumption of a hot maize porridge.

Laryngeal cancer has a high incidence in Thailand and may turn out to be not unconnected with a local cigar which contains uncured home-grown tobacco and tree bark in roughly equal proportions.

And there are even hints of a correlation between cancer of the colon and rectum and the consumption of meat. This environmental emphasis is expected to continue.—L.H.N.

MEETING NOTICES

The information on this "notices" page is offered as a service to all specialty groups and allied health agencies in order to publicize postgraduate educational opportunities available to subscribers. The deadline for publication in Connecticut Medicine *is the tenth of the month PRECEDING date of issue. Send copy to: Connecticut State Medical Society, 160 St. Ronan Street, New Haven, Connecticut 06511.*

GENERAL

April 27-29, 1971—Tuesday-Thursday
Connecticut State Medical Society
179th Annual Meeting of the Connecticut State Medical Society
Hilton Hotel, Hartford, Connecticut

CARDIOLOGY

May 13-15, 1971—Thursday-Saturday
7th Annual Cardiovascular Symposium
St. Francis Hospital, 114 Woodland Street, Hartford, Connecticut

INTERNAL MEDICINE AND SURGERY

September 15-June 1—Tuesdays
Lecture Series: "Medical Emergencies"
Lawrence and Memorial Hospitals, New London, Connecticut
Contact: Edward Gipstein, M.D., Director of Medical Education. (442-0711 ext. 361).

January 7-9, 1971—Wednesday-Friday
National Conference on Cancer of the Colon and Rectum
Hotel del Coronado, San Diego, California
Contact: American Cancer Society, 219 East 42nd Street, New York, New York 10017.

January 13-15, 1971—Wednesday-Friday
Coronary Atherosclerotic Heart Disease
Emory University School of Medicine, Altanta, Georgia
Contact: American College of Physicians, Philadelphia, Pennsylvania 9104

January 14, 1971—Thursday
Annual Meeting of the Connecticut Chapter American College of Surgeons.
Hotel Sonesta, Hartford, Connecticut

January 18-22, 1971—Monday-Friday
Recent Advances in Internal Medicine
Medical College of Georgia, Augusta, Georgia
Contact: American College of Physicians, Philadelphia, Pennsylvania

PSYCHIATRY

Lecture Series:
January 13, 1971—Wednesday **10:30 A.M.**
"Drugs and the Law"
John Donnelly, M.D.
January 19, 1971—Tuesday **10:30 A.M.**
"Suicide"
William Zeller, M.D.
Connecticut Valley Hospital
Merritt Hall
Middletown, Connecticut

CONNECTICUT CHAPTER
AMERICAN COLLEGE OF SURGEONS

JANUARY 14, 1971
HOTEL SONESTA—HARTFORD

Afternoon Program

Symposium on Emergency Room Care

Speakers will include a hospital administrator, a full time director of emergency services, a fiscal intermediary, a lawyer.

Evening Program

"Man and So Called Thermal Pollution"
by Daniel Merriman, Ph.D.

Assistant Professor of Biology at Yale and Director of Sears Foundatoin for Marine Research.

Science News

Animal-To-Human Infection

(*JAMA*, 213: 1559, September 7, 1970, Chapman, John S.) In the face of serious infectious disease one needs to question in a most searching fashion habits—hunting, fishing, camping—occupation in specific terms, and all accidental or intentional contact with either domesticated or wild animals, including rodents and birds.

Pets, both indoor and outdoor, can play a role as reservoirs of disease. The dog can spread toxocara canis infestation to children. He may become infected with tuberculosis from humans and then disseminate it. Cats spread catscratch fever.

Household birds spread psittacosis and tuberculosis. So can turkeys. Houses and pens used for bird raising are sources of human histoplasmosis. Swine or fowl may also spread atypical tuberculosis. Pigeons have caused an epidemic of human histoplasmosis. Glanders has largely disappeared, but Q fever occurs sporadically among employees of abattoirs.

Earlier epidemic diseases have been spread by nondomesticated animals: plague, typhus, rabies. Rodents contaminate soil with Coccidioides immitis while rickettsial pox is spread by mice. Tularemia, Rocky Mountain spotted fever and relapsing fever reach man via insect vectors or directly from animals.—L.H.N.

Normal-Pressure Hydocephalus

(*JAMA*, 213: 1615, September 7, 1970 James, A. E., Jr., et al). This disease is characterized by neurological symptoms of dementia and awkwardness of movement, cerebrospinal fluid pressure in the normal range, and ventricular enlargement without cortical atrophy.

Pneumoencephalograms reveal enlarged ventricles with failure of air to pass over the cerebral convexities. Cisternographic abnormalities are the presence of radioactivity in the enlarged ventricles, abnormality of movement of the injected radioactivity over the cerebral hemispheres, and failure of the radioactivity to concentrate in the sagittal area on delayed scans.

Normal-pressure hydrocephalus is a treatable form of dementia and can be recognized by clinical manifestations, findings from lumbar puncture, pneumoencephalography, and cisternography.—L.H.N.

Controlled Trial Of Amantadine Hydrochloride in Parkinson's Disease

(*Lancet* 1970 1: 259, February 7, 1970). A double blind cross over trial of amantadine hydrochloride 200 mg daily and placebo given for 2 weeks was conducted on thirty-seven outpatients with Parkinson's disease.

Thirty-five patients completed the trial and gave a highly significant preference for amantadine. Factors of history and physical examinations were assessed by means of a standard questionnaire and all features showed a superficial improvement in score on amantadine except for the parients assessment of their walking ability and the observers examination of rigidity.

The degree of improvement was not related to age, sex, duration or severity of disease, previous thalamolysis or concurrent indications.

Amantadine is probably similar in its mode of action to L-dopa and although the amount of benefit may be less with amantadine, the drug was free of side effects and was well tolerated by all patients in the trial.—L.H.N.

Methysergide Therapy Leads To Vascular Side-Effects

(*JAMA*, 213: 1571, September 7, 1970). Methysergide therapy for migraine and other vascular headaches can lead to inflammatory fibrosis in patients reported Dr. R. S. Kunknel to American Association for the Study of Headache. Seven of his patients developed retroperitoneal fibrosis due to methysergide. Their renal function returned to normal after discontinuing the drug.

Three cases developed significant valvular disease and in one, rheumatic valvular disease grew worse. Another patient, a 43 year old man developed severe angina after taking methysergide 1-2 tablets a day for 2 years.

Many explanations have been offered for the way in which the drug induces fibrosis but no definite mechanism has been pinpointed.—L.H.N.

Heat to Dilate Veins

In addition to dilating, the hot-towel technic can recanalize previously thrombosed veins if applied four to five times a day for three to four days. There are situations in which conservation or recanalization of veins can be life saving. However, the water and hot towel technic is cumbersome and requires considerable attention from a busy nursing staff.

Someone should develop a modern equivalent of the hot towel that is easy to use and thermostatically controlled so as to be safe for the patient.—L.H.N.

Hospital Costs Increase

Total expenses among the 5,820 community hospitals in the United States increased 17.2% during 1969 according to *Hospitals,* the Journal of the American Hospital Association.

The cost of hospital supplies, facilities and equipment increased by 26% in 1968 to 6.9 billion in 1969—while the cost of personnel increased by 11.9% from 9.2 to 10.3 billion.

Total increased expenses have been 13 to 16% per year since 1966.—L.H.N.

How to Spot Hijackers

(*Nature,* 227, 548, Aug. 8, 1970). As each passenger approaches the boarding area he is scrutinized for certain behavioral traits. Armed with this and "any other information" about the subject presumably what can be gleaned from his passport and the appearance of his baggage the operators of the test are able to give positive clearance to about 99.5 per cent of the passengers without holding them up at all.

The remaining 0.5 per cent are asked to walk past an array of magnetometers to see how much metal they are carrying. This second test generally clears about half of the suspects, the remainder of whom are interviewed.

Those to whom positive clearances can still not be given are researched and if nothing is found may be refused permission to board the aircraft. The method is not foolproof but 13 airlines now use the system and the rate of highjacking has been on the decline whereas in the rest of the world it continues unabated.

It was devised by Dr. John T. Darley, a psychologist with the Federal Aviation Administration in Washington.—L.H.N.

Human Digits in Organ Culture

(*Nature,* 227, 621, Aug. 8, 1970). These authors report a technique for growing human digits in a fluid synthetic medium containing serum. When first planted the embryo human rudiments each consisted of a cartilagenous rod. After 6 days of cultivation the digits had elongated by 20-60 per cent and growth in length then ceased.

Thus embryonic human fingers grown in organ culture in a fluid medium should provide valuable material for investigating the morphological and biochemical effects of various physiological and pathological conditions.—L.H.N.

The Incidence of Staining of Permanent Teeth by the Tetracyclines

(*Can. Med. Ass. J.* 103, 351, 1970). Of 238 subjects whose hospital records indicated ingestion of stated doses of tetracyline some 49 were seen to have staining of teeth which was confirmed by fluorescence and a further 6 had staining which did not fluoresce.

A definite relationship between total dosage and staining and duration of administration and staining was established. The condition occurred with greater frequency (in more than one third of the children) when the total dosage exceeded 3 grams or the duration of treatment was longer than 10 days.

However, as staining was seen at all dosage levels whatever the duration, physicians should prescribe other antibiotics where possible for children under 8 years of age or for women in the last trimester of pregnancy.—L.H.N.

Cholera Epidemic: Tip of the Iceberg

(*Nature,* 227, 766, Aug. 22, 1970). There is a cholera epidemic in the south of the Soviet Union. It started in Celebes in 1960 and spread through India, Pakistan, South-East Asia and now the USSR.

Progress on the treatment and prevention of cholera remains slow. With good diagnosis and facilities, the death rate of infected persons can be reduced from 60 per cent to 1 or 2 per cent. There has been heartening progress in the treatment of various complications such as those of the liver.

One difficulty of prevention is the short duration of immunity conferred by the present vaccines. It seems to be effective roughly in half of those treated and its effects persist only for about 6 months.

Much work remains to be done on the identification of cholera carriers in the population. Attention is now also directed to the epidemiology of the disease and the incidence of immunity in populations in which cholera is endemic.—L.H.N.

From the

Connecticut Regional Medical Program

Henry T. Clark Jr., M.D., Director

On November 9 the Connecticut Regional Medical Program submitted to Washington its 1970 Annual Report, Continuing Grant Request for 1971, and Request for a Supplemental Grant. The process by which each program activity was studied and/or site visited, rated as to level of performance and priority of importance to program goals, and finally recommended or disapproved for funding by the 20-member Review and Evaluation Committee has been described in a letter from its chairman, Robert U. Massey, M.D., to the CRMP Executive Committee and Advisory Board.

Dr. Massey, Associate Dean for Graduate Education at the University of Connecticut Medical School and Chief of Staff at the Newington VA Hospital noted that 44 projects in five program areas were reviewed—either by progress report alone (12), or by progress report and site visit (32)—as a step toward the preparation of the 1970 Annual Report and Continuing Grant Request for 1971. An additional five requests for new funds were examined for the development of the Request for a Supplemental Grant. All five requests were site visited.

The Review and Evaluation Committee, Dr. Massey reported, met on September 15 and on October 1, 15, 17, and 22, each session lasting from six to eight hours. "To insure fair and thorough review of all projects, several operational decisions were made."

—The 49 projects were divided into five program areas: Research and Evaluation, Health Service Area Program Assistance, University-Community Hospital Partnerships, Clinical Services, and Health Profession Education. Review panels were assigned to each program area.

—Each panel, assisted by a CRMP staff member assigned to it, made tentative decisions regarding site visit planning. Some projects which were terminating in 1970 were judged not to require site visits unless some questions were to arise after study of the progress reports.

—A format was developed for reporting project evaluation and recommendations to the CRMP Executive Committee. Each panel was to develop its recommendations for those projects within its purview and submit reports to the entire Review and Evaluation Committee for its modification and final action.

—Each committee member would then rate the individual projects in terms of relevance to the CRMP program as a whole. Ratings were by secret ballot on a 1-5 (poor to excellent) scale.

Dr. Massey wrote: "Site visit teams were made up of committee members, with one serving as chairman, plus consultants knowledgeable in areas related to the project content, and a staff member. The Review and Evaluation Committee has come to regard the site visit as an essential element in the review and evaluation process. Data are acquired during these visits which clarify and supplement the information in the project proposal or the progress report. Attitudes of project participants, enthusiasm for the project or apparent lack of it, level of institutional commitment and willingness to work out cooperative arrangements with other institutions and resources become apparent during the dialogue of the site visit. Finally, the site visitors can assist in transmitting a clearer picture of CRMP goals to the project representatives, and may suggest developments in the project or relations to other projects which may help in the over-all program evolution.

"In general, the committee believes the program which is evolving in CRMP is good. There was enthusiasm for many projects and a feeling of satisfaction that CRMP could help in fostering such efforts. Other projects were seen as promising, but still obviously developmental. Still others seemed less clearly related to CRMP program goals, or rather weak in design. These varying judgments regarding the 49 projects should be obvious from the reports. The Committee has sensed in itself a growing ability to recognize what clearly is in keeping with CRMP grand design, and what may or may not be."

"Finally, I would like to take this opportunity to commend members of the Review and Evaluation Committee for their hard work and high level of interest and commitment, not only during this last cycle of review, but also since the appointment nine months ago. I calculate that they have spent upwards of 2,000 man hours in this activity. Recent meetings have, I believe, demonstrated a level of sophistication which will enable this Committee to approach with confidence its third role, 'to consider how the larger objectives of CRMP can be implemented, and make appropriate recommendations to the Executive Committee."

An appreciation of the value of the Committee's collective judgment in evaluating CRMP projects and goals may be gained by a look at its membership:

ROBERT MASSEY, M.D., Chairman
Associate Dean, Graduate Education
University of Connecticut School of Medicine
Chief of Staff, Newington VA Hospital
JOSEPH J. SMITH, M.D., Vice-Chairman
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BOOK REVIEWS

OBSTETRICAL ANESTHESIA. Current Concepts and Practice. Sol M. Shnider, Editor. 256 pages, Introduction by Stuart C. Cullen, M.D. Williams and Wilkins Co., Baltimore, Maryland, 1970.

Reviewed by: FREDERICK W. HEHRE

This latest short text on obstetrical anesthesia is an excellent compendium edited by Sol M. Shnider, M.D. from contributions by 14 individual writers. Among them are well recognized authorities in the field, including Bonica, Moya, Flowers and Shnider himself.

The book is divided into five sections: (1) Physiology and Pharmacology; (2) Anesthesia for Normal Vaginal Delivery; (3) Anesthesia for Obstetrical Difficulties; (4) Complications of Obstetrical Anesthesia: Etiology, Prevention and Therapy and (5) Perinatology and the Anesthesiologist. Each section is subdivided into chapters in which the individual contributors discuss relative and specific problems, including drugs and anesthetic techniques, in his own area of expertise. The chapters are refreshingly short, clear, succinct and authoritative in style. The bibliographical references following each chapter contain not only very pertinent articles but also some very recent and timely ones.

This reviewer felt that the sections on obstetrical difficulties and the complications of anesthesia were particularly noteworthy; but that the chapters on fetal heart rate, fetal scalp sampling and the treatment of fetal distress were unfortunately superficial. For example, the bibliography of 10 articles following the chapter on fetal heart rate contains nine references to the work of Caldeyro-Barcia's group and only a single one to Hon's work.

The volume is clearly printed on good quality paper and is easily readable. It is well suited for the personal library of every anesthesiologist who practices obstetrical anesthesia, as well as to departmental libraries of obstretrics and gynecology.

DISABILITY IN ANTIQUITY. Fareed Haj, Philosophical Library, New York, N.Y. 1970. 188 pp. $6.50.

Reviewed by: VICTOR L. SZANTON

Dr. Fareed Haj, a native of the Middle East, has a B.A. in Arabic, English and Philosophy from the University of London and a Ph.D. from the New York University School of Education, with rehabilitation counseling as his major. His interest in the specific history of the Middle East as related to the view of disabling disease is, therefore, natural and understandable. In this book "Disability in Antiquity" he limits his material to the Middle East in the Middle Ages. His pursuit of this theme impresses one, particularly with the chapter devoted to the disabilities through war. He states "The history of no other nation can record more battles than the Arabs. To them war was alternately a sport, an economic necessity, a business enterprise and a religious duty. It was also their greatest tragedy". He goes on, "during the last 10 years of the Prophet's life the Moslems engaged in fifty war enterprises, civil wars, wars over personalities, wars against outsiders". Among the results of these engagements, the loss of sight was the greatest single lasting disability. Battles resulted in tremendous numbers of fatalities since not many soldiers, wounded, lived long enough to receive medical attention.

Blindness was at all times a common disability. Its prevalence yielded the Middle East physician their superior knowledge of eye diseases. Loss of eyesight was not only the result, of warfare but also of diseases: leprosy, trachoma, smallpox cataracts, ophthalmia. It also resulted from penal ocular enucleation.

Mutilation as punishment was customarily inflicted. All extremities were subject to amputation including the tongue. Listing of this goes on and on throughout the text. There is no mention of rehabilitation, of prosthetic devices, or of methods of coping with disabilities.

This volume is an exposition of the horror of the Arab world during the Middle Ages through war, neglect and inhumanity. Scholarly it is not. It is reportorial and as such reflects the mystique of the Middle Ages:—that for the man who follows the religion of war, the supreme value is strife—a stance hopefully out of date, wishfully out of time and optimistically out of mind.

GAS CHROMATOGRAPHY IN BIOLOGY AND MEDICINE: A Ciba Foundation Symposium. Edited by Ruth Porter. J. & A. Churchill, Ltd., London, 1969. pp. 213 with 67 illustrations.

Reviewed by: ROY N. BARNETT

This is another of the Ciba Foundation Symposia in which 25 participants, leaders in their field, discuss the newest developments in a specific discipline. In this case gas chromatography, described by Dr. S. R. Lipsky of Yale as—"the most powerful technique ever devised", is the subject. There is an entrancing "historical background" by Prof. A. J. P. Martin, the inventor of the method. The sensitivity of gas chromatography, particularly when combined with mass spectrometry and computer analysis is expressed strikingly by Dr. A. S. Curry as follows: "In just over two years, therefore, the sensitivity of absolute identification available as a routine service in the Forensic Science Service in the U.K. has been increased by a factor of about 10,000—from 100 g. to 1 ug. using trapped gas chromatographic fractions and micro i.r. spectrometry and to less than 10 ng. using the gas chromatography—mass spectrometry combination". Somewhat parenthetically he continues; "This can be called a "recent development"; it certainly stresses the value of the British system of forensic science which is nationally organized by the Home Office and so allows capital expenditure on a scale not possible for the organizational systems of other countries."

Although much of the volume is devoted to technical aspects of the separation of chemicals by gas and liquid chromatography, and to identification of small quantities of the separated materials, there are also several discussions of medical applications of the technique. These include blood gas analysis, forensic toxicology, aircraft accident toxicology and anesthetic gas detection. An intriguing section by Lowe and Hagler from the University of Chicago described, among other subjects, an automated system for anesthesia in which the level of anesthetic agent in the body determines the rate of delivery of additional anesthetic.

The work is interesting in the frontier-of-science aspect of medicine but is not recommended to the general physician audience.

Connecticut Medicine

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Index to Advertisers

Arch Laboratories — — — — — — — — — — — 909
Campbell Soup Company — — — — bet 892 & 893
Classified Advertisement — — — — — — — — — 918
Dentocain Company — — — — — — — — — — — 909
Arthur W. Eade — — — — — — — — — — — — IBC
Geriatric Pharmaceutical — — — — — — — — — 2
Group Insurers, Inc. — — — — — — — — — — — 909
Hynson, Westcott & Dunning, Inc. — — — — — — 3
Lederle Laboratories — — — — — — — — — — — 5
Eli Lilly & Company — — — — — — — — FC & 10
McNeil Laboratories, Inc. — — — — — — — — — 873
A. H. Robins Company, Inc. — — 876, bet 876 & 877 & 877, bet 908 & 909
Roche Laboratories — — — — — — — — — — — BC
Sanibel Hospital, Inc. — — — — — — — — — — — 6
Schering Corporation — — — — — — — — 912 & 913
G. D. Searle — — — — — — — — — — — bet 892 & 893
Smith, Kline & French Laboratories bet 892 & 893
Stuart Pharmaceuticals — — — — — — — — — — 8 & 9
Upjohn Company — — — — — — — — — 868, 869, 870

Connecticut Medicine
Connecticut State Medical Journal

. . INDEX . .

Volume 34 December, 1970

A

Alkalosis Due To Carter's Little Pills, Hypokalemic Metabolic (Ramirez and Marieb) iii 169
Anemia, Methimazol Induced Aplastic (Rosenberg) i 32
Anemia, Post-Myocardial-Infarction Syndrome With (Glasser) vi 413
Anesthesia, Newer Thoughts On Obstetric (Hook) x 696
Anesthesiology Grand Rounds vii 512, viii 580, x 735
Anesthesiologist, Professional Liability Of (Manthey and Murphy) x 714
Anesthetic Agents, Interactions Between Certain Drugs Used Preoperatively And (Daniels) x 708
Aneurysm, Hypothermia For Excision of Hepatic Artery (Lerner, Toole and Hehre) i 40
Aneurysm, Technical Aspects of Surgical Management Of A Right Hepatic Artery (Toole, Stern, Lerner and Lowman) ix 619
Annual Meeting, Program—178th iii 165, iv 241
Antibiotics In Central Nervous System Infections, The Intrathecal and Intraventricular Administration (Quintiliani) v 321
Around The State i 66, ii 138, iii 210, iv 276, v 373, vi 433, vii 528, viii 591, x 748 xi 830, xii 916
Art Exhibition, Connecticut Physicians vii 531
Arteries, Transposition Of The Great (Anagnostopoulos, DeLeuchtenberg, Talner, Stansel, Jr.) viii 573
Arthritis, Serum Antinuclear Antibodies In Rheumatoid (Hughes and Rothfield) iii 171
Arthritis Of The Sternoclavicular Joint Due To Coliform Bacillus, Acute (Delevett and Monahan) ix 629
Artists, Attention iii 168, iv 252
Auditing Of Physicians' Records (Streich) vii 515

B

Books In Review, New ii 140, iii 217, vi 458, vii 522, viii 599
British National Health Services (Thomas) i 60, ii 128, iii 198, iv 291, v 365, vi 444

C

Cancer Incidence, Mortality And Survival In Connecticut During The 1960's (Christine, Sullivan, Connelly, Foote) viii 564
Cancer, The Use of Drugs in Various Types of Cancer (Fischer) xii 903
Cardiac Surgery, Anesthesiology And The Newborn For (Gilman) vii 496
Cardiac Surgery In Infancy (Stansel, Jr.) vii 500
Catheters, Misplaced Central Venous Pressure (Schweizer and Foster) xi 802
Child Abuse, JeJunal Hematoma, And Felson's Sign (Bratu, Dower, Siegel and Hosney) iv 261
Connecticut Regional Medical Program v 370, vi 446, vii 529, viii 587, ix 659, x 750, xi 829, xii 922
CSMS Staff Members, New ix 638
Coronary Defects, Surgical Correction Of Congenital (Ogden) ix 626
Correspondence v 377, vi 442, vii 526, viii 586, ix 656, x 742

D

Delivery Of Medical Care For The State of Connecticut Council Approves Position Paper On ix 639
Doctor's Office ii 125, v 376, ix 655, xi 820

E

Electrocardiography, Clinical Application of Atrial Pacing Stress (Leach, Jr. and McLean) xii 839
Electrocardiogram Of The Month i 58, ii 132, iii 196, iv 284, v 362, vi 436, vii 520, viii 584, ix 646 x 740, xi 824, xii 910
Endocarditis In The Drug User (Andriole) v 327
Esophageal Atresia By End-To-Side Anastomosis And Ligation Of The Tracheo-Esophageal Fistula, Operative Management Of (Touloukian and Pickett) xi 783
Executive Director's Office, From The i 52, ii 120, iii 201, iv 265, v 355, vi 417, vii 505, ix 633, x 728, xi 814, xii 886

EDITORIALS

- Acoustic Trauma From Rock And Roll iv 228
- Agriculture, Methods For Pest Control In xi 765
- Alcohol, Effect Of, On The Blood i 9
- Alcoholism As A Business Problem, Drug Ahuse Overtaking xi 763
- Alcoholism, The Biology Of xi 757
- Amniocentesis In Prediction Of Chromosomal And Behavioral Abnormalities i 10
- Anesthesiology, Recent Progress In viii 549
- Arterial Thrombosis, The Effect Of Aspirin On iii 159
- Arthritis, Rheumatoid, When Is Rheumatoid Arthritis v 312
- Astronauts, Adaptations In, To Interplanetary Space Flights viii 546
- Air Pollution, The "Hard" Costs Of xii 881
- Atherosclerosis, Carbon Monoxide And, viii 554
- Britain, Unheard Voices Of Surgeons In, v 298
- British Clinician Speaks, A viii 553
- Calcium Malabsorption With Advancing Age xii 874
- Cancer, Prevention Of x 670
- Cancer Tests, Diagnostic Progress In xi 759
- Cancer Research, The Government Downgrades x 685
- Chromosome, Tracking The Y x 684

Clinical Laboratory, A Look Into The Future Of The iv 235
College Grades, Prediction From x 683
College Students, How Much Superstition In Our xi 777
Compensation For Time And Skill Versus Compensation For Procedures ix 608
Congenital Defects, Environmental Causes Of xi 776
Coronary Care Unit Of A Community Hospital, Medical Coverage In A iii 153
Coronary Heart Disease, The Effects Of Physical Training In iii 148
Coronary Patient, Drugs, Dreams And The vi 385
Courts Will Help To Resolve The Environmental Crisis vi 386
Death, Sudden, What The Doctor Can Do In Solving The Problem i 8
Detergents, Side Effects Of, iv 237
Dreaming Sleep, Effect Of Some Drugs On i 1
Dying Patient, Doctor And The ix 613
Earth Day—April 22, 1970 ix 607
Ectopic Beats More Dangerous Than Others iii 152
Education, Continuing xii 883
Education Of The Infant And Young Child i 12
Electrocardiography And The Family Physician vii 472
Encephalitis, Idoxuridine (IDU) In Herpesvirus Hominis v 303
Environmental Degradation, Case Histories, In i 14
Environmental Quality, Facts And Recommendations, Report of The Council x 677
Environmental Studies: An Institution For, Redesigning The Environment vi 391
Family Physician—A New Specialist ii 76
Family Planning, Can Alone Solve The Population Explosion ii 82
FDA, The: Harnessing The Scientific World For Its Important Cause ix 605
Fertility Control, New Approaches To, vii 461
Fertility, Controlling Human, viii 541
Financial Pinch On Science vi 399
Gestation, Movements of The Human Fetus During xi 757
Genetic Factors, Serum Cholesterol And Cardiovascular Disease i 6
Goiter Due To Iodide Ingestion By The Mothers, Fetal x 685
Health Care, The Role Of The Government ii 74
Heart Attacks, The Winter Toll of xii 882
Heart Disease Under Different Stresses, The Town Driver With ii 81
Heart Valves, Growing Ones Own vii 466
Heroin Plague viii 544
Herpes Virus And Its Multifarious Clinical Expression, The Illusive x 675
Hospital Law, Decisions In iv 224
Hunger and Malnutrition In The United States ix 601
Hyperoxygenation, Improving Cognitive Function In i 2
Hypertension, A Physiologic Approach To The Treatment Of Essential vii 468
Hypertensive, To Treat Or Not To Treat The Mild viii 542
Hypertensives, Survival In Treated iv 226
Hyperthyroidism, The Role of Sympathetic Blockade In The Treatment Of, viii 547
Impotence, Androgen Function And xii 878
Influenza, Horse, And The Human Hong Kong Strain i 10
Interferon And Interferon Inducers, On ii 85
Interferon, The Widening Spectrum Of Therapeutic Uses Of, vii 468
Intestinal Physiology, Some Complexities Of Small vi 394
Lithium Carbonate In Affective Disorders iii 160
Lung Disease, Chronic Obstructive ii 86
Lupus Erythemotosus Syndrome, Drug Induced xii 875
Man, Reflections On Aggression In ii 80
Manpower, Retirement Can Be A Waste Of, viii 542
Marihuana: I xi 766
Marihuana: II xii 871
Medical Education, Reflections On Continuing vii 474
Medical Science And Practice In The Next Decade vi 390
Meditation, Psysiologic Changes During Transcendental v 300
Methadone: Rehabilitation Without A Cure vii 462
Microbiology, Some Global Impacts Of Applied iii 155
Monitoring, A look Into The Future Of Patient, iv 238
Moon Dust, The iv 232
Multiphasic Screening In The Next Decade iii 146
Obesity, Hazards Of, i 16
Office Laboratory, Peer Evaluation Of The xi 778
Pacemaker, When To Use A Transvenous Catheter vi 393
Papilliary-Muscle Dysfunction Syndrome, The iv 236
Parkinson's Disease: Amantadine In: An Instance of Medical Serendipity xii 880
Parkinsonism, L-Dopa In vi 396
Patient Is Also A Person, The vii 478
Peptic Ulcer, Diet In, Medical Dogma ii 87
Pesticides, Problems and Hazards Of xi 768
Physical Fitness, Isometric Exercises And, v 304
Pill and Wishful Thinking, Psychopathology Of The ix 611
Pneumonia—Going From Cure To Prevention, Vaccines Against ix 617
Pollution, The Global Effects Of Environmental ii 88
Protein Synthesis, Senescence And Errors In iii 162
Psychotic Disorders In The Community ix 602
Pulmonary Disease, Exercise Training For The Patient With Chronic Obstructive vi 395
Renal Calculi vii 470
Respiratory Tranct Disease, The Outlook For Control of Acute xii 867
Rhythms In Man, Circadian v 314
Science Tools: Tubeless Gastric Analysis By The Heidelberg Capsule xii 879
Septicemia, Gram Negative x 679
Sex Determination Reconsidered ix 616
Sleep: A New Bridge Between Psyche And Soma x 669
Sleep Cycles, Clinical Implications Of The, v 307
Society, A Look Into The Future Of ii 73
Surgical Practice, Differences In Patterns Of, v 316
Survival, Developing A Science For, A Look Into The Future of Society iii 145
Thermal Regulation, The Tympanic Thermometer And, iv 230
Thrombophlebitis, Infusion ix 610
Thyroid Hormone, Norepinephrine Turnover In Brain After Administration Of Imipramine: Enhancement By, vii 465
University In Medicine, The Role Of The iv 221
Viral Infections, Control Of, The Chemical Approach iii 161
Viruses, Cross Reactions Of Oncogenic viii 550

Viruses And Cancer: Herpes Virus Vaccine Protects Against Marek's Disease of Chickens vi 398
Vitamin E. Deficiency x 688
Warfare, Some Consequences Of Chemical And Biological v 318
Water Pollution Abatement xi 772
Water Pollution, Steps Taken To Abate Air and Cleaning Up Our Environment v 297

E

Esophageal Atresia By End-To-Side Anastomosis And Ligation Of The Tracheo-Esophageal Fistula, Operative Management Of (Touloukian and Pickett) xi 783

F

Family Physician Of The Future, A Curriculum For Training The, (Mignone) ii 91
Femoral-Tibial Bypass: Salvage of Ischemic Lower Extremities With Inadequate Popliteal Runoff (Fenn and Alderman) xi 796

G

Gigantism, Hereditary Pancellular Lysosomal, Chediak-Higashi Syndrome) (Flynn, Jr., Coley, Beckett, Danes) viii 557

H

Heart Disease In Infancy, The Radiological Diagnosis of Congenital (Fishbone) vii 490
Heart Disease, The Newborn Intensive Care Unit For Infants With (Campbell) vii 481
Heart Disease, Recognition And Diagnosis Of The Infant With Critical Congenital, (Talner) vii 486
Hepatic Amebiasis: Current Viewpoints In Diagnosis And Therapy (Siderides and Strauch) ii 96
Hepatic Resections, Current Controversies Surrounding Major (Strauch) xi 792
Hodgkin's Disease, Splenectomy As An Adjunct To the Treatment (Nuland) xii 851
Hodgkin's Disease, The Management Of (Vera, Prosnitz, Fischer and Kligerman) xii 856
Hodgkin's Disease, The Yale Combination Chemotherapy Program For Advanced (Levitt, DeConti, Pearson, Marsh, Zanes, Mitchell, Kaetz and Bertino) xii 862
House Of Delegates, Summary of Proceedings Of The ii 118, vi 426
Hypoglycemia, Diagnosis and Management Of (Felig, Sachs, Landsberg, Brooten) iii 185

I

Immunosuppressive Agents, The Pharmacology Of (Mitchell, and Bertino) xii 843
Intrauterine Transfusion II, Fetal (Wade, Ogden and Davis) i 21

J

Jaw, The Fractured (Goldberg, Nemarich, Aslanian) viii 570

L

Laboratory Notes ii 131, vi 453
Law-Medicine Notes v 367, vi 439, vii 523, viii 583, ix 654, xi 819
Life, First Sixty Minutes of (Cordero, Jr.) x 701
Lithium Toxicity, A Case Of Manic-Depressive Illness With (Sachs and Landsberg) i 36
LSD Adverse Effects Of (Greenblatt and Shader) xii 895
Lung, Reliability Of Diagnostic Tests In Patients With Carcinoma Of The (Morhardt and Montgomery) iii 177
Lymph Node Biopsy and Mediastinoscopy, An Experience With Pre-Scalene (Dineen and Patel) xi 789

M

Medical Grand Rounds i 36, iii 185, iv 277, ix 649
Medical Profession And The Press (Gough) iv 287
Medicine In Israel (Thomas) ix 644
Meeting Notices i 70, ii137, iii 216, iv 295, v 376, viii 596, ix 663, x 754, xi 835, xii 919
Memoriam, In:
  Antupit, Louis ix 662
  Beaudry, Joseph H. i 69
  Borkowski, Boleslaus vii 511
  Brown, Abe S. i 69
  Buckley, John W. ii 136
  Calef, Bension vii 511
  Clark, William T. v 379
  Conroy, Michael J. ii 137
  Dayton, Arthur B. i 69
  Dayton, Theodore R. v 379
  De Angelis, Louis R. xi 827
  DeCristoforo, Ralph xii 894
  Deming, Clyde L. i 69
  Dinan, Henry P. ix 662
  Drake, Leo Berthier xi 827
  Duennebier, Harold W. viii 590
  Fabricant, Milton W. vi 448
  Flanagan, Edwin D. vi 448
  Frank, Harry S. iii 214
  Friery, Clarence Milton, Sr. xi 827
  Griswold, Matthew H. i 69
  Hinckley, Elizabeth Brennan xii 894
  Iasiello, Emilio P. viii 590
  Jackson, Allen F. xii 894
  Jones, Robcliff Vesey vii 511
  Karpel, Saul xi 827
  Kligerman, Martin James xi 827
  Larrabee, John W. ii 138
  Little, Milton F. v 379
  Lombardi, Pasquale F. ii 137
  Marranzini, Samuel xii 894
  Metcalf, Elliott H. v 380
  Meyer, Fritz Martin xi 827
  Pomeroy, William Henry xii 894
  Priddy, Foster Eugene xi 827
  Roccapriore, Benjamin A. iii 214
  Segal, Jacob v 380
  Senfield, Maxon M. ii 137
  Simonton, Frank F. v 380
  Smith, Arthur C. vi 448
  Sturtevant, James Melvin vii 511
  Weinerman, Edwin R. v 380
  Weise, Ellwood C. ix 662
  Wilson, Frank E. vi 448
  Yeager, Charles F. v 380
  Zaglio, Edmond R. iii 214
  Zwick, Frank ii 137

Meningitis, Adrenocorticosteroid Therapy Of Bacterial (Thornton) v 331
Meningitis, Vaccination Against Meningococcal (Goldschneider) v 335
Muscle Relaxants And Some Problems With Their Use (Greenhouse) x 723

O

Obituaries:
  - Antupit, Louis xi 826
  - Blake, Eugene M. ii 136
  - Conroy, Michael J. iii 214
  - Jaffe, Samuel v 379
  - Larrabee, J. Whitfield iii 213
  - Nesbit, Robert R. xi 826
  - Segal, Jacob A. vi 447
  - Tuch, Morris i 69
  - Wilson, Charles C. vi 447

P

Parkinson's Disease, Pharmacodynamics of 3, 4-Dihydroxyphenylalanine (Dopa) In (Van Woert) vi 401
Physician's Placement Service i 65, ii 121, iii 208, iv 272, v 358, vi 421, vii 508, viii 588, ix 660, x 732, xi 817, xii 890
Pregnancy, Sacrococcygeal Teratoma Of The Fetus Complicating, (Pepe, Pyun and Katzenstein) vi 411
President, Address Of The vi 429
President's Page i 47, ii 116, iii 182. iv 250, v 354, vi 415, vii 504, viii 578, ix 631, x 727, xi 812 xii 837
Pseudocysts, Management of Complications Of (Vilinskas) ix 622
Psychosis Due To Talwin (Pentazocine), Acute Organic, (Yost, Jr. and McKegney) iv 259
Psychotropic Drugs, Ocular (Pigmentary) Effects Of (Appleton, Shader and DiMascio) i 25

R

Renal Transplantation, Problems In Cadavaric Donations For (Schiff, Jr., Lytton, Brown and Goffinet) iv 253
Respiratory Intensive Care (Gilman) x 719
Respiratory Infection, Usefulness Of Gram Stain And Routine And Quantitative Culture Of Sputum In Patients With And Without Acute (Bartlett and Melnick) v 347
Rheumatoid Carditis (Kra and Fazzone) iv 257
Rubella Vaccine—Some Perspectives (Lepow) v 340

S

Science News i 71, ii 123, iv 240, v 381, vi 454, vii 532, viii 597, ix 664, x 752, xi 831, xii 920
Scintillation Scanning In A Community Hospital: Part IV (Kay) ii 96
Secretary, Report Of The vi 431
Space Diets In Medicine viii 595
Sphincterotomy And Choledocholithiasis, Transduodenal (Whalen and Major) xi 810
Surgical Gloves, Puncture Wounds In (Butterfield) iii 180

T

Thyroid Therapy On The Hyponatremia And Hypoosmolality Of Myxedema, The Effect Of (Marieb, Ragaza and Al-Sadir) i 29
Trauma Patient: Results Of The Yale Trauma Study, A Methodology For Studying The Emergency Care Of The (Kreggi, Webb, Jr., and Broadbent) ii 107
Urinary Tract, Infection Of The (Lewis) v 343

V

Vaginal Antibiotic For Surgery (Cohen and DiSaia) vi 406

W

Wells, Horace, Dr. (Martin) x 694
Woman's Auxiliary i 63, ii 134, iii 212, iv 293, v 378, vi 449, vii 527, viii 592 x 745, xi 828, xii 915

X

X-Ray Of The Month i 45, ii 126, iii 193, iv 282, vi 434, vii 518, xii 914

Z

Zinc Story: An Introduction (Bradley) xi 805

. . INDEX . .

Volume 34 December, 1970

A

Alderman, Donald B. (with Fenn)
  Femoral-Tibial Bypass: Salvage Of Ischemic Lower Extremities With Inadequate Popliteal Runoff xii 796
Al-Sadir, Jafar (with Marieb and Ragaza)
  Thyroid Therapy On The Hyponatremia And Hypoosmolality Of Myxedema, The Effect Of i 29
Anagnostopoulos, C. E. (with DeLeuchtenberg, Talner and Stansel)
  Arteries, Transposition Of The Great viii 573
Andriole, Vincent T.
  Endocarditis In The Drug User v 327
Appleton, William S. (with Shader and DiMascio)
  Psychotropic Drugs, Ocular (Pigmentary) Effects Of i 25
Aslanian, Robert (with Goldberg and Nemarich)
  Jaw, The Fractured viii 570

B

Bartlett, Raymond C. (with Melnick)
  Respiratory Infection, Usefulness of Gram Stain And Routine And Quantitative Culture of Sputum In Patients With And Without Acute v 317
Beckett, Ronald S. (with Flynn, Coley and Danes)
  Gigantism, Hereditary Pancellular Lysosomal, (Chediak-Higashi Syndrome) viii 557

Bertino, Joseph R. (with Mitchell)
  Immunosuppressive Agents, The Pharmacology Of xii 843
Bertino, Joseph R. (with Levitt, DeConti, Pearson, Marsh, Zanes, Mitchell, Kaetz)
  Hodgkin's Disease, The Yale Combination Chemotherapy Program For Advanced xii 862
Bratu, Marcel (with Dower, Siegel and Hosney)
  Child Abuse, Jejunal Hematoma and Felson's Sign iv 261
Broadbent, Ernest J. (with Keggi and Webb, Jr.)
  Trauma Patient: Results Of The Yale Trauma Study, A Methodology For Studying The Emergency Care Of The ii 107
Bradley, Donald F., Jr.
  Zinc Story: An Introduction xi 805
Brown, Robert S. (with Schiff, Jr., Lytton, and Goffinet)
  Renal Transplantation, Problems In Cadavaric Donations For iv 253
Butterfield, William C.
  Surgical Gloves, Puncture Wounds In iii 180

C

Campbell, A. G. M.
  Heart Disease, The Newborn Intensive Care Unit For Infants With vii 481
Christine, Barbara (with Sullivan, Connelly, Foote)
  Cancer Incidence, Mortality And Survival In Connecticut During the 1960's viii 564
Cohen, Burton H. (with DiSaia)
  Vaginal Antibiotic For Surgery vi 406
Coley, Mary S. (with Flynn, Beckett and Danes)
  Gigantism, Hereditary Pancellular Lysosomal, (Chediak-Higashi Syndrome) viii 557
Connelly, Roger R. (with Christine, Sullivan, Foote)
  Cancer Incidence, Mortality And Survival In Connecticut During The 1960's viii 564
Cordero, Leandro, Jr.
  Life, First Sixty Minutes Of x 701

D

Danes, B. Shannon (with Flynn, Coley, Beckett)
  Gigantism, Hereditary Pancellular Lysosomal, (Chediak-Higashi Syndrome) viii 557
Daniels, John C.
  Anesthetic Agents, Interactions Between Certain Drugs Used Preoperatively And x 708
Davis, Clarence D. (with Wade and Ogden)
  Intrauterine Transfusion II, Fetal i 21
de Cholnoky, Tibor
  Mammaplasty, Present Status Of Augmentation xi 808
DeConti, Ronald C. (with Levitt, Pearson, Marsh, Zanes, Mitchell, Kaetz, Bertino)
  Hodgkin's Disease, The Yale Combination Chemotherapy Program For Advanced xii 862
DeLeuchtenberg, N. (with Anagnostopoulos, Talner, and Stansel)
  Arteries, Transposition Of The Great viii 573
Delevett, Allen F. (with Monahan)
  Acute Arthritis Of The Sternoclavicular Joint Due To Coliform Bacillus ix 629
DiMascio, Alberto (with Appleton and Shader)
  Psychotropic Drugs, Ocular (Pigmentary) Effects Of i 25
Dineen, Joseph P. (with Patel)
  Lymph Node Biopsy And Mediastinoscopy, An Experience With Pre-Scalene xi 789
DiSaia, Philip (with Cohen)
  Vaginal Antibiotic For Surgery vi 406
Dower, John C. (with Bratu, Siegel and Hosney)
  Child Abuse, Jepunal Hematoma and Felson's Sign iv 261

F

Fazzone, Philip (with Kra)
  Rheumatoid Carditis iv 257
Fenn, John E. (with Alderman)
  Femoral-Tibial Bypass: Salvage of Ischemic Lower Extremities With Inadequate Popliteal Runoff xi 796
Fisher, David S.
  Cancer, The Use of Drugs In Various Types Of Cancer xii 903
Fischer, James J. (with Vera, Prosnitz, Kligerman)
  Hodgkin's Disease: The Management Of, Evolution Of Radiotherapy Concepts xii 856
Fishbone, Gerald
  Heart Disease In Infancy, The Radiological Diagnosis Of Congenital vii 490
Flynn, Frederick J., Jr. (with Coley, Beckett and Danes)
  Gigantism, Hereditary Pancellular Lysosomal, (Chediak-Higashi Syndrome) viii 557
Foote, Franklin M. (with Christine, Sullivan, Connelly)
  Cancer Incidence, Mortality And Survival In Connecticut During The 1960's viii 564
Foster, James H. (with Schweizer)
  Catheters, Misplaced Central Venous Pressure xii 802

G

Gilman, James I.
  Cardiac Surgery, Anesthesiology And The Newborn For vii 496
Gilman, James I.
  Respiratory Intensive Care x 719
Glasser, Morton
  Anemis, Post-Myocardial-Infarction Syndrome with vi 413
Goffinet, John A. (with Schiff, Jr., Lytton, Brown)
  Renal Transplantation, Problems In Cadavaric Donations For iv 253
Goldberg, Morton H. (with Nemarich and Aslanian)
  Jaw, The Fractured viii 570
Goldschneider, Irving
  Meningitis, Vaccination Against Meningococcal v 335
Gough, Paul
  Medical Profession And The Press iv 287
Greenblatt, David J. (with Shader)
  LSD: Adverse Effects Of, A Current Perspective xii 895
Greenhouse, B. Barry
  Muscle Relaxants And Some Problems With Their Use x 723

H

Hehre, Frederick W. (with Lerner and Toole)
  Aneurysm, Hypothermia For Excision Of Hepatic Artery i 40
Hook, Robert
  Anesthesia, Newer Thoughts On Obstetric x 696
Hosney, Salah H. (with Bratu, Dower, Siegel)
  Child Abuse, Jejunal Hematoma, And Felson's Sign iv 261
Hughes, Grace D. (with Rothfield)
  Arthritis, Serum Antinuclear Antibodies In Reumatoid iii 171

K

Kaetz, Harvey W. (with Levitt, DeConti, Pearson, Marsh, Zanes, Mitchell, Bertino)
  Hodgkin's Disease, The Yale Combination Chemotherapy Program For Advanced xii 862

Katzenstein, Rolf E. (with Pepe and Pyun)
  Pregnancy, Sarcrococcygeal Teratoma Of The Fetus Complicating vi 411

Kay, Chester J.
  Scintillation Scanning In A Community Hospital: Part IV ii 96

Keggi, Kristaps, J. (with Webb, Jr. and Broadbent)
  Trauma Patient: Result Of The Yale Trauma Study, A Methodology For Studing The Emergency Care Of The ii 107

Kligerman, Morton M. (with Vera, Prosnitz, Fischer)
  Hodgkin's Disease: The Management Of, Evolution of Radiotherapy Concepts xii 856

Kra, Siegfried J. (with Fazzone)
  Rheumatoid Carditis iv 257

L

Landsberg, Lewis (with Felig, Sachs, Brooten)
  Diagnosis and Management Of Hypoglycemia iii 185

Leach, Charles N. (with McLean)
  Electrocardiography, Clinical Application of Atrial Pacing Stress xii 839

Lepow, Martha L.
  Rubella Vaccine—Some Perspectives v 340

Lerner, Samuel M. (with Toole and Hehre)
  Aneurysm, Hypothermia For Excision Of Hepatic Artery i 40

Lerner, Samuel M. (with Toole and Stern)
  Technical Aspects Of Surgical Management Of A Right Hepatic Artery Aneurysm ix 619

Levitt, Martin (with DeConti, Pearson, Marsh, Zanes, Mitchell Kaetz, Bertino)
  Hodgkin's Disease, The Yale Combination Chemotherapy Program For Advanced xii 862

Lewis, George W.
  Urinary Tract, Infection Of The v 343

Lowman, Robert (with Toole, Stern and Lerner)
  Technical Aspects Of Surgical Management Of A Right Hepatic Artery Aneurysm ix 619

Lytton, Bernard (with Schiff, Jr., Brown and Goffinet)
  Renal Transplantation, Problems In Cadavaric Donations For iv 253

Mc

McKegney, Patrick (with Yost, Jr.)
  Psychosis Due To Talwin (Pentazocine), Acute Organic iv 259

McLean, Charles E. (with Leach, Jr.)
  Electrocardiography, Clinical Application of Atrial Pacing Stress xii 839

M

Major, James W. (with Whalen)
  Sphincterotomy And Choledocholithiasis, Transduodenal xi 810

Manthey, Frank A. (with Murphy)
  Anesthesiologist, Professional Liability Of x 714

Marieb, Norman J. (with Ragaza and Al-Sadir)
  Thyroid Therapy On The Hyponatremia And Hypoosmolality Of Myxedema, The Effect Of i 29

Marieb, Norman J. (with Ramirez)
  Alkalosis Due To Carter's Little Pills, Hypokalemic Metabolic iii 169

Marsh, John C. (with Levitt, DeConti, Pearson, Zanes, Mitchell Kaetz, Bertino)
  Hodgkin's Disease, The Yale Combination Chemotherapy Program For Alvanced xii 862

Martin, Steven J.
  Wells, Dr. Horace x 694

Melnick, Avrohm (with Bartlett)
  Respiratory Infection, Usefulness Of Gram Stain And Routine And Quantitative Culture Of Sputum In Patients With And Without Acute v 347

Mignone, Joseph
  Family Physician Of The Future, A Curriculum For Training The ii 91

Mitchell, Malcolm S. (with Bertino)
  Immunosuppressive Agents, The Pharmacology Of xii 843

Mitchell, Malcolm S. (with Levitt, Deconti, Pearson, Marsh, Zanes, Kaetz, Bertino)
  Hodgkin's Disease, The Yale Combination Chemotherapy Program For Advanced xii 862

Monahan, David T. (with Delevett)
  Acute Arthritis Of The Sternoclavicular Joint Due To Coliform Bacillus ix 629

Morhardt, Charles E. (with Montgomery)
  Lung, Reliability Of Diagnostic Tests In Patients With Carcinoma Of The iii 177

Murphy, William R. (with Manthey)
  Anesthesiologist, Professional Liability Of x 714

N

Nemarich, Albert (with Goldberg and Aslanian)
  Jaw, The Fractured vii 570

Nuland, Sherwin B.
  Hodgkin's Disease Splenectomy As An Adjunct To The Treatment Of xii 851

O

Ogden, John A. (with Wade and Davis)
  Intrauterine Transfusion II, Fetal i 21

Ogden, John A.
  Surgical Correction Of Congenital Coronary Defects ix 626

P

Patel, Jashwant (with Dineen)
  Lymph Node Biopsy And Mediastinoscopy, An Experience With Pre-Scalene xi 789

Pearson, Howard A. (with Levitt, DeConti, Marsh, Zanes, Mitchell, Kaetz, Bertino)
  Hodgkin's Disease, The Yale Combination Chemotherapy Program For Advanced xii 862

Pepe, Vincent (with Pyun and Katsenstein)
  Pregnancy, Saerococcygeal Teratoma Of The Fetus Complicating vi 411

Pickett, Lawrence K. (with Touloukian)
  Esophageal Atresia By End-To-Side Anastomosis And Ligation Of The Tracheo-Esophageal Fistula, Operative Management Of xi 783

Prosnitz, Leonard R. (with Vera, Fischer, Kligerman)
  Hodgkin's Disease: The Management Of, Evolution Of Radiotherapy Concepts xii 856
Pyun, Kyum S. (with Pepe and Katzenstein)
  Pregnancy, Sacrococcygeal Teratoma Of The Fetus Complicating vi 411

Q

Quintiliani, Richard
  Antibiotics In Central Nervous System Infections, The Intrathecal And Intraventricular Administration Of v 321

R

Ragaza, Edgardo P. (with Marieb and Al-Sadir)
  Thyroid Therapy On The Hyponatremia And Hypoosmolality Of Myxedema, The Effect Of i 29
Ramirez, Basilia (with Marieb)
  Alkalosis Due To Carter's Little Pills, Hypokalemic Metabolic iii 169
Rosenberg, Arthur H.
  Anemia, Methimazol Induced Aplastic i 32
Rothfield, Naomi F. (with Hughes)
  Arthritis, Serum Antinuclear Antibodies In Rheumatoid iii 171

S

Sachs, Frederick Lee (with Landsberg)
  Lithium Toxicity, A Case of Manic-Depressive Illness With i 36
Schiff, Martin, Jr. (with Lytton, Brown and Goffinet)
  Renal Transplantation, Problems In Cadavaric Donations For iv 253
Schweizer, Robert T. (with Foster)
  Catheters, Misplaced Central Venous Pressure xi 802
Shader, Richard I. (with Appleton and DiMascio)
  Psychotropic Drugs, Ocular (Pigmentary) Effects Of i 25
Shader, Richard I. (with Greenblatt)
  LSD: Adverse Effects Of, A Current Perspective xii 895
Siderides, Lambros E. (with Strauch)
  Hepatic Amebiasis: Current Viewpoints In Diagnosis And Therapy ii 96
Siegel, Bernard (with Bratu, Dower and Hosney)
  Child Abuse, Jejunal Hematoma, And Felson's Sign iv 261
Stansel, H. C., Jr.
  Cardiac Surgery In Infancy vii 500
Stansel, H. C., Jr. (with Anagnostopoulos, DeLeuchtenberg, and Talner)
  Arteries, Transposition Of The Great viii 573
Stern, Harold (with Lerner, Lowman and Toole)
  Technical Aspects Of Surgical Management Of A Right Hepatic Artery Aneurysm ix 619
Strauch, Gerald O. (with Siderides)
  Hepatic Amebiasis: Current Viewpoints In Diagnosis And Therapy ii 96
Strauch, Gerald O.
  Hepatic Resections, Current Controversies Surrounding Major xi 792
Streich, Arnold J., L.L.B.
  Auditing Of Physicians' Records vii 515
Sullivan, Paul D. (with Christine, Connelly, Foote)
  Cancer Incidence, Mortality And Survival In Connecticut During The 1960's viii 564

T

Talner, Norman S.
  Heart Disease, Recognition And Diagnosis Of The Infant With Critical Congenital vii 486
Talner, N. S. (with Anagnostopoulos, DeLeuchtenberg, and Stansel)
  Arteries, Transposition Of The Great viii 573
Thomas, Ned
  British National Health Services i 60, ii 128, iii 198, iv 291, v 365, vi 444
Thomas, Ned
  Medicine In Israel ix 644
Thornton, George F.
  Meningitis, Adrenocorticosteroid Therapy Of Bacterial v 331
Toole, Allen L. (with Lerner and Hehre)
  Aneurysm, Hypothermia For Excision Of Hepatic Artery i 40
Toole, Allen L. (with Stern, Lerner and Lowman)
  Technical Aspects Of Surgical Management Of A Right Hepatic Artery Aneurysm ix 619
Touloukian, Robert J. (with Pickett)
  Esophageal Atresia By End-To-Side Anastomosis And Ligation Of The Tracheo-Esophageal Fistula, Operative Management Of xi 782

V

VanWoert, Melvin H.
  Parkinson's Disease, Pharmacodynamics of 3, 4-Dihydroxphenylalanine (Dopa) In vi 401
Vera, Raul (with Prosnitz, Fischer, Kligerman)
  Hodgkin's Disease, The Management Of, Evolution Of Radiotherapy Concepts xii 856
Vilinskas, J.
  Management Of Complications Of Pancreatic Pseudocysts ix 622

W

Wade, Maclyn E. (with Ogden and Davis)
  Intrauterine Transfusion II, Fetal i 21
Webb, Samuel B., Jr. (with Keggi and Broadbent)
  Trauma Patient: Results Of The Yale Trauma Study, A Methodology For Studying The Emergency Care Of The ii 107
Whalen, William A. (with Major)
  Sphincterotomy And Choledocholithiasis, Transduodenal xi 810

Y

Yost, Murray A., Jr. (with McKegney)
  Psychosis Due To Talwin (Pentazocine), Acute Organic iv 259

Z

Zanes, Robert P. (with Levitt, DeConti, Pearson, Marsh, Mitchell, Kaetz, and Bertino)
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